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VOL. 43 JANUARY 1955 Fasc. 1

ACTA RADIOLOGICA

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ACTA RADIOLOGICA
EDITA IUSSU SOCIETATUM RADIOLOGICARUM
DANIAE, FENNIAE, NORVEGIAE ET SUECIAE

VOL. 43 JANUARY 1955 FASC. 1

SUBLUXATION AND DEFORMATION OF THE CERVICAL APOPHYSEAL JOINTS

A contribution to the aetiology of headache

by

Ákos Kovács

Cervical cephalea, the majority of migraine cases, 'cervical migraine', and the upper cervical sympathetic syndrome described by Barré-Lieau, are patterns undoubtedly belonging to the same clinical entity. The syndrome has been examined in detail by Bartschi-Rochaix and in his monograph (1949) attention is called to its various forms.

In the group of the diseases of the cervical roots, ganglia, and sympathetic nerves, much discrepancy has been found between the clinical features and roentgenologic signs by numerous authors (Bull, Bartschi-Rochaix, Thomsen, Reischauer), whereas the bone changes are not considered significant. In our view, roentgenologists have the opportunity of throwing more light upon this problem; they should by a more detailed examination of the cervical spine be able to separate the processes resulting in contraction from those unrelated to nerves and vessels. They should, by paying greater attention to the rôle of the time factor, recognize those changes produced by defensive mechanisms, for instance, bone destruction (Kahlau and Duus). Finally, they should recognize signs of contracting processes due to lesions not directly visualized roentgenologically (protrusion, herniation, thickening of ligaments).

Great progress in this field was accomplished by Bartschi-Rochaix when he introduced tomographic examination of the unco-vertebral borderlines and emphasized the significance of cervical osteochondrosis by pointing out the formerly neglected signs arising from the autonomous nervous system.

Brain (1952), in discussing the discrepancy between the myelographic and the conventional roentgen method, stated that as far as the former

Submitted for publication, 15 February 1954.

From the Roentgen Department (Director: Ákos Kovács) of Rokus Hospital, Budapest, Hungary.

a. b. c.

Fig. 1. Model of the vertebral artery. (a) Artery in front. (b) Artery behind. The articular process of C II does not reach the artery. (c) Vertebrae out of line; subluxation. The articular process reaches the artery and compresses it against the lower border of the transverse process.

is concerned, the posterior borderline osteophyte is the most reliable sign. A similar claim was made in respect to the lumbar region by the author of this paper (1949) who described osteophytic formation surrounding the herniated disk.

The rôle of the posterior borderline osteophyte as a factor in the syndrome was also recognized by FRYKHOLM. In his unselected autopsy material on adult subjects posterior borderline osteophytes were covered by calcified fibro-cartilaginous tissue which formed the major part of the protruding ridges. HADLEY discussed the sequelae of contracted foramina and the degeneration of roots and ganglia occurring in spondylarthrosis and osteochondrosis.

In this paper we shall deal with subluxations of the small joints resulting in constriction or circulatory disturbance in the vertebral artery and impaired function of the plexus symp. vert. By subluxation we mean the displacement of contiguous articular surfaces rather than the irreparable changes in the vertebrae and articular processes reported by HADLEY in which the articular process, as a result or independently of trauma, is, over a period of years, built up into a new shape and increased in size (Fig. 1).

Anatomy

The vertebral artery arises from the upper and posterior part of the subclavian artery. After a short course in front of the transverse process of the 7th cervical vertebra it enters the foramen in the transverse process of the 6th vertebra, ascends through the foramina up to the transverse process of the atlas, and finally passes through the arch of the atlas and the foramen magnum into the skull. On the ventral surface of the medulla oblongata the right and left vertebral arteries join to form the basilar artery. Its major branches are the two cerebellar arteries and the

posterior cerebral artery. It may be superfluous to stress its importance. Along with the internal carotid artery, it furnishes one-sixth of the cardiac output to the brain representing 2 per cent of the entire body weight. The diameter of the artery being not more than 4 to 5 mm, the blood contained by it flows at a greater velocity than the average. The latter fact may be due to its course representing the prolongation of the blood stream in the ascending aorta. It is a peculiar feature of this artery that it passes, unlike any other vessel, through five bony foramina situated at a distance of 2 cm from each other and by which it is to some extent fastened (Fig. 2). Behind the artery and vein the spinal ganglion is seated in the sulcus nervi spinalis and posterior to the ganglion lies the superior articular process of the corresponding vertebra. The distance between the artery and the apex of the articular process running upwards and forwards is hardly more than 2 to 3 mm; its distance from the posterior vertebral border varies between 3 and 6 mm. In women as well as in men of a gracile somatotype the transverse processes lie in a frontal plane and the line joining the right and left articular processes runs behind the vertebral body. In larger vertebrae the 'transverse' processes run slightly forwards and the line mentioned passes through the posterior part of the vertebra (Fig. 2). The more transverse the course of the transverse processes the more posterior, thus nearer to the articular processes, lie the artery and the nerve. These relations, as will be explained later, form an aetiologic factor of the diseases under consideration.

Fig. 2. The site of the vertebral artery is determined by the transverse process.

Pathology

The artery and nerve (vertebral sympathetic plexus) are rather frequently affected by the deformities of adjacent bone borders. Arterial damage due to the broadening of the unco-vertebral borders was reported by BARTSCHI-ROCHAIX (1949). In his necropsy material, FRYKHOLM (1951) found a lateral protrusion causing a distinct indentation of the artery. HADLEY examined the spine of individuals suffering from severe spondylosis or spondylarthrosis (1951) and found considerable deformities and transformations of the articular processes (termed 'subluxation' in

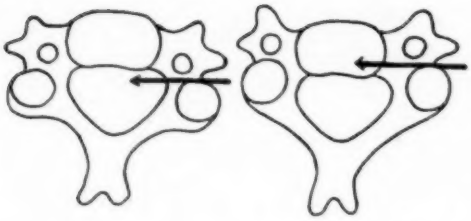


Fig. 3. In slender vertebrae, the line connecting the articular processes runs behind the vertebral body. In larger vertebrae, the vertebra is crossed by this line. In the former case the possibility of the articular process reaching the artery, is greater.

his paper). The caption to one of his films (12) points out the close relationship between the nerve roots and the vertebral artery. The present author described a lesion of the sympathetic nerves passing through the intervertebral foramina as early as in 1938. BELLÁK has suggested that headache might be due to lesions of the articular processes giving rise to arterial stenosis. OVERTON and GROSSMANN (1952) in a report on 36 necropsies stated that varieties allowing irregular movements frequently occur in the cervical spine mainly in the 2nd and 3rd vertebrae. Distortion of the articular process was found in 18 cases, broadening due to degeneration in 4, and absence of the uncinate processes in one case. In 1941, the present author called attention to the fact that the plane constituted by the articular surfaces of C II and C III is, in comparison with the other articular surfaces, rotated slightly backwards round the vertebral axis. In the illustrations of the paper of OVERTON and GROSSMANN, two deformities of the articular surface are noteworthily present and form a complete obstruction to the circulation of the vertebral artery. These deformities are not mentioned in the paper.

Subluxation may be due to chondrosis or traumata. The chondrosis may result in functional disorder of the unit termed motion segment (Bewegungssegment) by JUNGHANNS. The accompanying muscle defence will result in spinal deformity, firstly in the form of increased lordosis, followed by a compensatory erect posture. Later, the capsule ligament of the small joint becomes overloaded and the superior articular surface begins to slip slowly downwards and backwards on the oblique inferior articular surface, and subluxation arises. The backward displacement is limited by the arch of the vertebra. Frequently, impaction of the slipped superior articular surface leads to an atrophic excavation or hole made by the lower extremity of the articular process (Fig. 4). In other cases the site of the impaction is surrounded by an elevation, that is to say, an osteophyte. A similar buffer-osteophyte may arise on the lower margin of the transverse process. These changes are of a compensatory character (Figs. 5 and 6). The posture produced by the failure of compensation is either lordotic or the axis of the spinal column forms an angle. Frequently, the upper vertebra is also displaced backwards and the posterior vertebral borders become out of line (Figs. 1c and 14a).

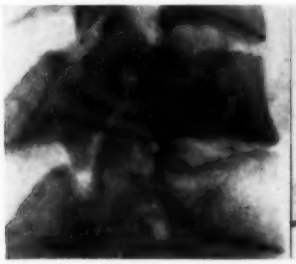


Fig. 4.

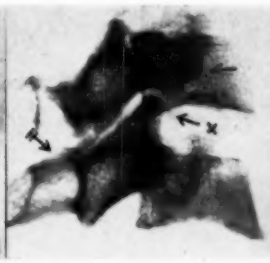


Fig. 5 a.

b.

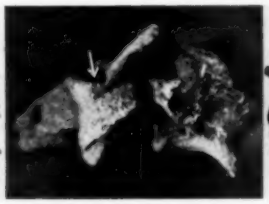
Fig. 4. The lower articular process of the vertebra slipping backwards strikes against the underlying arch. At the site of the impaction there is an excavation due to pressure atrophy.

Fig. 5. (a) and (b). Osteophytic growth downwards from the edge of the (←) transverse process prevents the articular process (X) reaching the artery (←). At the lower border slipping is prevented by a rampart (⌒→).

The demonstration of subluxation at necropsy is rather difficult. Roentgenograms obtained post mortem constitute no evidence since there is no basis for the contention that the post-mortem conditions are identical with those produced under the effect of muscle tension. Still a sign exists which permits of the conclusion that a subluxation may have been present for a long time. It is a well-known fact that the pulsation of vessels adjacent to bones results in the destruction of its substance (impression of the meningeal arteries, aneurysms of the aorta, etc.). In the cervical vertebrae a bony excavation of similar origin not infrequently occurs on the anterior surface of the superior articular processes and is due to pressure exerted by the vertebral artery in cases of subluxation (Fig. 7). This arterial impression was seen in 6 of our 54 cases.

Deformity of the articular process following spondylarthrosis and spondylarthritis are less difficult to recognize (Figs. 6 and 8). Naturally,

Fig. 6 a.



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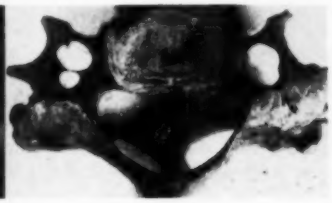
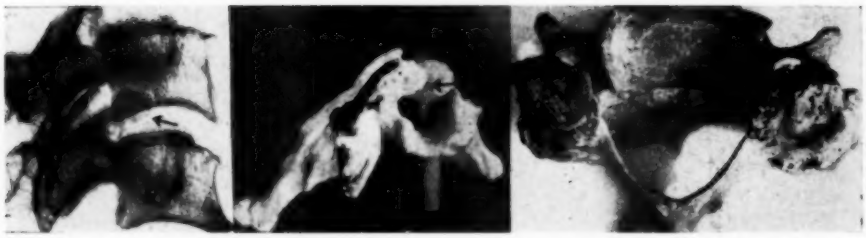


Fig. 7

Fig. 6. (a) and (b). The prolonged articular process reaches the artery. The formation of the rampart (⌒→) was late.

Fig. 7. Impression of the artery on the upper articular process.



a. b. c.

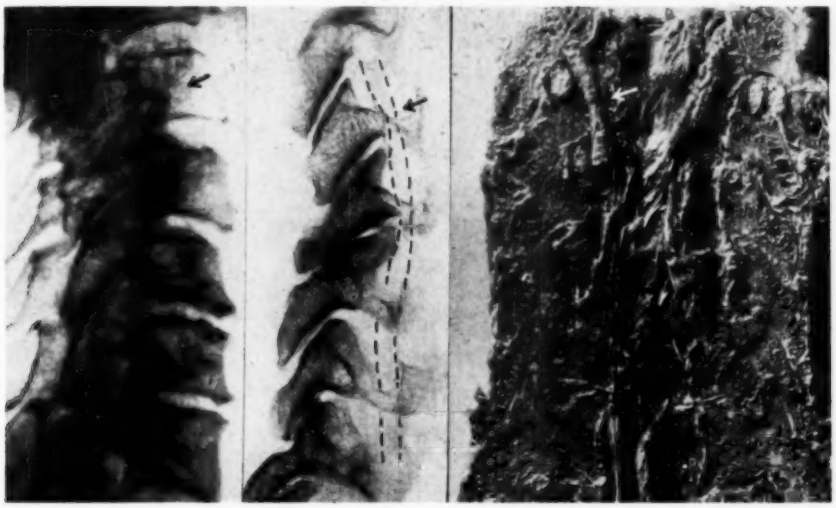
Fig. 8. (a), (b) and (c). Spondylarthrosis. The foramen transversarium is nearly completely covered by the broadened articular process.

they may be attended by subluxation. In the preparation shown in Fig. 8, the site of the artery and nerve is partly covered by the marginal proliferation of one of the articular processes. This is particularly well seen if the articular process is visualized through the foramen transversarium. The broadening due to spondylarthrosis of the articular surface is essentially the result of failure of repair, and aims at restricting the increased mobility and instability beyond the earlier limits by means of the broader joint surface. The inertia of nature results in the morbid process passing beyond the 'aim' because the broadening of the joint surface will, in addition to restricting movement, irritate, and later paralyse, the sympathetic plexus and further interfere with the circulation of the vertebral artery either directly or by producing vasospasm.

In one of our patients the opportunity arose of examining a severely distorted articular process post mortem.

Case 1. E. D., a woman, aged 72, had for many years suffered from cervical pain radiating into the arms, cardiac pain of an anginal type, and headaches. She had had polyarthritis 40 years previously. The headaches gradually became intolerable. Finally the patient died from heart failure in status asthmaticus.

A film covering the region from C IV to C VII revealed a considerable narrowing of the cartilaginous disks as well as broadening, deformity and greater steepness of the articular surfaces of the small joints, and much narrowing of the spaces. Between C V and C VI there was a lipped border suggesting the presence of a small hernia (Fig. 9a). The roentgen examination for function failed to show evidence of flexion or extension. In addition, C IV and C V were some millimetres out of line. Large osteophytes and lipping were observed on all the posterior margins. A film of the intervertebral foramina showed that they were narrowed. Some weeks after this examination the patient died. A film of the cervical spine obtained post mortem was identical with a similar view obtained during life (Fig. 9b). The sawn preparation showed the extent to which the roentgenologic examination of the living patient was reliable. In agreement with the film, the broadening of the joints, the downward flexion of the uncinate processes, and the subsequent broadening of the bony border of the vertebra and narrowing of the cartilaginous disks and interspaces, were revealed. The removal of the arches demonstrated that the functional defi-



a. b. c.

Fig. 9. (a). Distorted and broadened articular processes of C IV and C V below the protruding transverse process (↑). Protrusion of the disk between C V and C VI; posterior borderline lips (↑). (b) Film of the dissected spine. Broadening of the vertebrae posteriorily, elongated and distorted articular processes protruding below the transverse process causing funnel-shaped constriction of the artery in two places. (c) Photograph of the spine, with the upper contraction well shown; the lower one has been destroyed by the saw.

ciency due to the failure of the shrunken disks gave rise to a process of a compensatory character consisting in a broadening of C V and C VI around the disk hernia. The body of the vertebra became broadened by about one-fourth of its original size with concomitant narrowing of the vertebral canal by about one-fifth of its diameter. This contraction might not have produced any serious effects except for a slight disturbance of the CSF circulation. Finally, we found a millet-sized protrusion between C VI and C VII which was not seen in the films obtained in vivo or in the dissected cervical spine but appeared only in the film taken of the sawn preparation. The superior articular process of C IV and C V protruded below the transverse process and, by exerting pressure on the nerve and the artery, caused a funnel-shaped contraction of the latter (Fig. 9d). The corresponding foramen was naturally also considerably contracted. The film obtained of the separated joints (Fig. 9b) well demonstrates the articular processes, thickened and distorted as a result of the polyarthritis and the degenerative cartilage disease.

Method of Examination

The cervical portion of the spinal column is readily accessible to roentgenology. The examination should be carried out with the patient sitting, the film being enclosed in a flexible container and slightly pressed

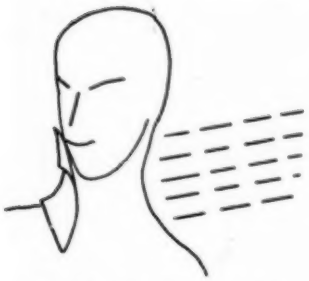
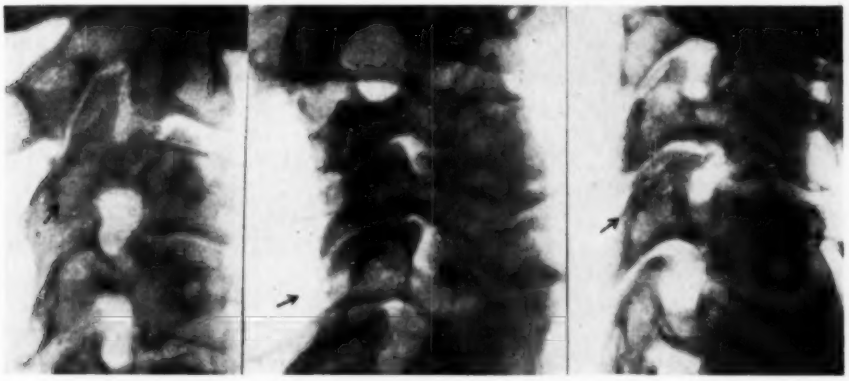


Fig. 10. Roentgenographic technique.

against the neck (Fig. 10). The spinal column of a patient lying on his side cannot be straightened and the cassette is at a too great distance from the bone with consequent blurring of detail. Thus the film-holder should be adaptable, and held by a rubberized linen band or by the patient himself. SCHOEN's apparatus may also be employed for the lateral views and rapid serial films of the foramina; this will permit accurate centring and the application of a load (Glisson's traction) if necessary both in flexion and extension.

1) *Lateral view.* The articular processes should be projected upon one another and any difference in registration not exceed 3 mm. The film taken in extension shows the degree of the approximation to the vertebral artery by the articular process. A film is then obtained with anteflexion of the neck and horizontal Glisson's traction. The anteflexion should be performed by the examiner. While the anteflexion combined with some traction is being carried out one or more cracks may be heard as a sign of the reduction of subluxations evident in the films. The patient may experience temporary relief of his headache and not infrequently it may be lasting. If, however, it is transient the 'anteflexion sign' lends great support to the diagnosis, indicating that the pressure increase present within the foramen may be relieved by dilatation. In other cases the film taken in anteflexion shows that the forward projection of the transverse process is moderate (Fig. 1), the articular processes also remain behind and the posterior border of the vertebra is free and clearly visible. In these cases calcification of the posterior ligaments and hernias of calcified cartilage may be visible.

2) *Representation of the intervertebral foramen.* The central ray, in line with the axis of the short foraminal canal, should run from behind forwards and towards the side to be examined. It constitutes an angle of from 35° to 40° with the frontal plane, a greater one (from 50° to 55°), with the sagittal plane, and, being directed forwards and downwards, an angle of 10° to 15° with the horizontal plane. If these conditions have been observed, the anterior and posterior tubercles of the transverse process will lie outside the area of the foramen (Fig. 11). Similarly, the lunate process, running upwards, coincides with the margin of the foramen but does not project into it. If the film has been taken with the proper technique these anatomic structures may be readily differentiated from morbid ones, such as a distorted processus lunatus or a calcified herniated



a. b. c.

Fig. 11. Film of the intervertebral foramen. There is hardly any space below the transverse processes where the broadened articular processes are seated. The canal for the nerve root is nearly obturated.

disk. Since GUTZEIT, WENT, DUUS, KAHLAU, REISCHAUER, PILLOKAT and other authors have claimed that, apart from diseases of the intervertebral roots, secondary irritation of the cervical ganglia may also lead to organ lesions and functional disorders, the significance of the representation of the foramina has greatly increased. The course of the vertebral artery may be traced on the films and the broadened or subluxated articular processes demonstrated, so that this view will confirm any changes evident in the lateral film (Fig. 11).

3) *The antero-posterior roentgenogram or tomogram* may sometimes show the broadening of the unco-vertebral borderline (BARTSCHI-ROCHAIX).

4) *Representation of the foramen transversarium.* The patient should be seated in the position as for the lateral view. The central ray is directed upwards, at an angle of about 30° with the horizontal plane, towards the foramen transversarium. The view is of particular value when the transverse process is 'hanging', if it is lying horizontally the borders of the excavation will be shown.

5) *Tomography* may, in doubtful cases, eliminate errors due to incorrect projection.

The question whether or not the articular process is in contact with the vertebral artery cannot be answered without a latero-lateral film in extension. The film of the foramen, and one obtained at an angle of 45°, show the forward displacement or broadening of the process. These films,

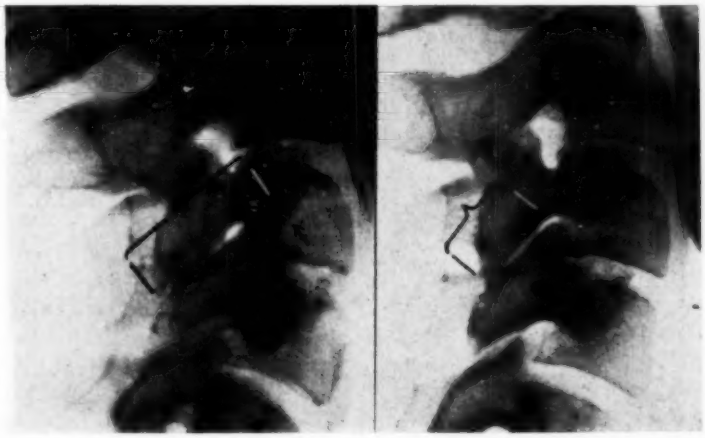
however, will but rarely and only in extreme cases demonstrate whether the process reaches as far as to the artery. Out of 40 examinations, we encountered only 6 cases in which this was seen to have occurred. The constrictions of the foramina of the upper vertebrae may then result in occipital neuralgia and combined patterns may arise. In the majority of cases the transverse process curves downwards (Fig. 5a), and the articular process striking against this downward curving portion cannot reach the artery; it may, however, frequently appear in the film of the foramen in the situation of the artery. An accurate lateral view cannot therefore be dispensed with; in this latter the situation of the artery can easily be located; it lies at the deepest point of the sulcus nervi spinalis (Fig. 2). If the articular process, besides touching the margin of the transverse process, should reach this point the diagnosis is assured. In doubtful cases, the examination may be augmented by the view of the foramen transversarium.

The *neurologic*, *otologic* and *ophthalmologic* signs of the syndrome are discussed in detail in the monograph of BARTSCHI-ROCHAIX. One further sign readily elicited during the roentgen examination should be mentioned. This sign was reported by the present author in 1938 and later (1944) by SPURLING. Vertical pressure exerted on the head resulting in pain radiating into the shoulders and arms (increased pressure upon the roots) may, in cases of subluxation, be evaluated in a negative sense. Apparently, the pressure exerted by the articular process on the artery does not always produce direct pain whereas the relief which occurs upon upward traction of the head is rather characteristic. This sign may be used in preliminary examinations for the differentiation of pain caused by pressure upon the nerve root, or the artery. Of course, mixed cases may also occur in which the sign has little value.

Cases

Case 2. B. F., male, aged 55, with unilateral dull headaches of constant character occurring two or three times in every month, by day or night, mostly on the left side. Each attack lasted for 8 to 10 hours, sometimes for several days, and was unrelieved by drugs. Examination of the urine, blood count and sedimentation rate, as well as roentgenograms of the skull were negative. The region below the second spinous process was tender to pressure. The headache increased on downward pressure upon the head and ceased on anteflexion-traction.

Roentgen examination of the cervical spine. The film obtained during a headache showed increased lordosis of the upper cervical region and the posterior borders of C III and C IV out of line, C III being displaced a few millimetres backwards. The left superior articular process of C IV was seen to protrude below the transverse process above it. The articular processes were in contact over an area of 26 mm (Fig. 12a). The film taken in anteflexion-traction showed that the space below the transverse process, *i. e.* the site of the vertebral artery, was free and the area over which the articular processes were in contact was only 15 mm (Fig. 12b). In this position the headache ceased. It could be brought on again by moving the head backwards. The patient was given a special pillow



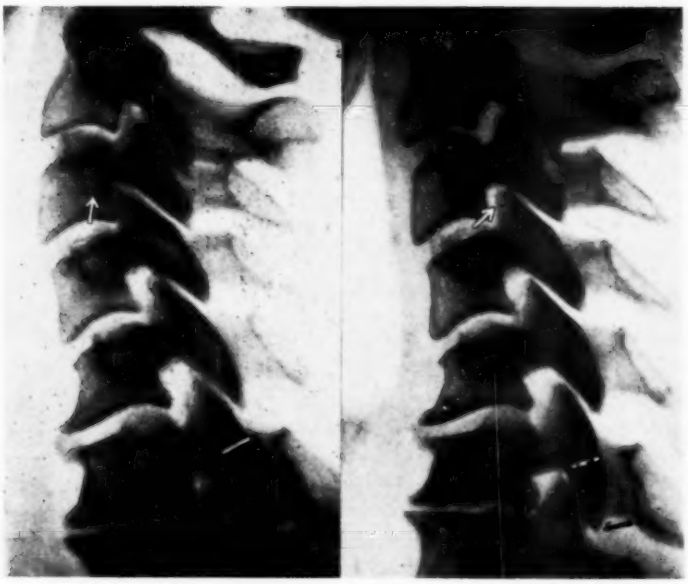
a. b.

Fig. 12. (a) Film taken during the headache. The left upper articular process of the C IV is below the transverse process. (b) After reduction; the headache ceased.

to immobilize his head during sleep; in the course of 9 months the headache occurred only once and ceased immediately following reduction of the affected joints.

Case 3. G. A., female, aged 43, had had headaches for 8 years; these, as a rule, occurred in the morning ('after sleeping in a certain position') and extended over the whole head. In the previous two years she had paresthesia and pain radiating to the arms. Her hands were weak. In the previous three months the small joints of the fingers had become swollen and stiff; this was attributed to chronic polyarthritis. All clinical examinations were negative.

Roentgen examination. The lateral view of the cervical spine showed that the lordosis had changed to a defensive erect posture (Fig. 13a). There was evidence of slipping of the small joints of C II, C III and C IV so that the upper articular processes of C III and C IV approximated to, although they did not touch, the transverse processes. The disk lying between the C VI and C VII was compressed and there was a small area of calcification above its posterior margin (protrusion); the articular processes had slipped. The film taken in anteflexion-traction showed the reduction of the subluxation (Fig. 13b), the distance between the articular and transverse processes, and a decrease of the surface along which the inferior articular processes were in contact from 19 to 10 mm. This difference of 9 mm, with due allowance for distortion due to the projection, represented a significant liberation of the constricted intervertebral foramina. During the manipulation of the neck two loud cracks were heard. They were followed by immediate relief of pain and headache. The manipulation was repeated upon several occasions. The decrease in the intensity of the cracks produced suggested that the reduction was becoming effective, and a fortnight later this was confirmed by roentgenology. The swelling of the joints of the hands had disappeared and after a long period of rest, the patient resumed her occupation. No doubt, the artery was in this case affected by the subluxation of the superior articular processes whilst the nerve root and the accompanying sympathetic plexus were being injured by the dislocation of the inferior articular processes.



a. b.

Fig. 13. (a) The upper articular process of C III, and especially C IV, are near the respective transverse processes. The articular processes of C VI and C VII in subluxation. (b) Reduced; no headache.

Case 4. T. G., female, aged 55, had had occipital headache for one year. The pain extended as far as the frontal region and occurred every day in the form of attacks.

Roentgen examination. Lateral view of cervical spine taken during an attack showed that C III and C IV were about 8 mm out of line. The superior articular processes of C IV and C V protruded below the transverse processes above (Fig. 14a). Anteflexion-traction resulted in relief and disappearance of subluxation as shown roentgenologically (Fig. 14 b).

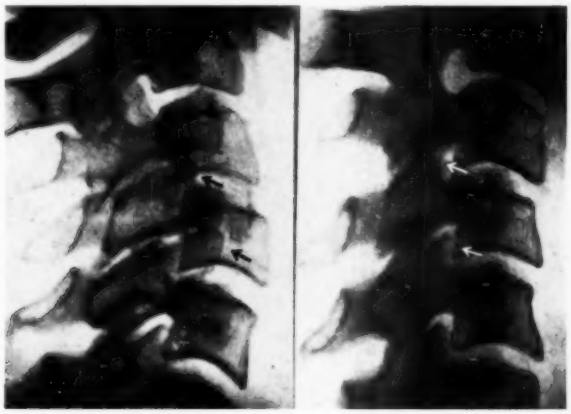
Case 5. R. J., male, aged 52, had suffered from constant headache for two months. Relief only occurred during sleep. He had recently also had pain radiating into the right arm. Clinical examinations were negative. Anteflexion-traction resulted in immediate relief.

Roentgen examination. The lateral film of the cervical spine showed increased lordosis and a distorted (wedge-shaped) disk between C III and C IV. There was also narrowing of the interspaces of the small joints between C II and C III and between C III and C IV, and thickening of the extremities of the articular processes. The articular processes of C III and C IV protruded to below the corresponding transverse processes (Fig. 15a). The film of the right intervertebral foramina showed that there was no space to accommodate the vertebral artery (Fig. 15b). Thus, spondylarthrosis and subluxation were the factors producing the syndrome.

Glisson's traction, massage, and rest in bed, resulted in the disappearance of the symptoms within a week.

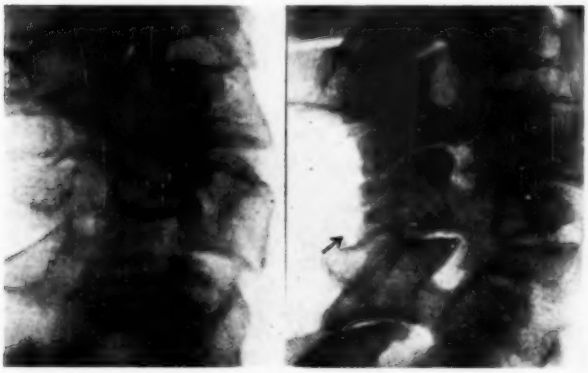
Case 6. C. P., female, aged 56, complained of headaches, neuralgic pain in the arms and cardiac pain of several months' duration.

Roentgen examination. The upper articular process of C IV protruded below the transverse process. The transverse process of C V was approximated by the corresponding articular process (Fig. 16a). Anteflexion-traction resulted in the disappearance of the subluxation (Fig. 16b).



a. b.

Fig. 14. (a) C III and C IV out of line. Superior articular processes of C IV and C V below the transverse processes. (b) Reduction; no headache.



a. b.

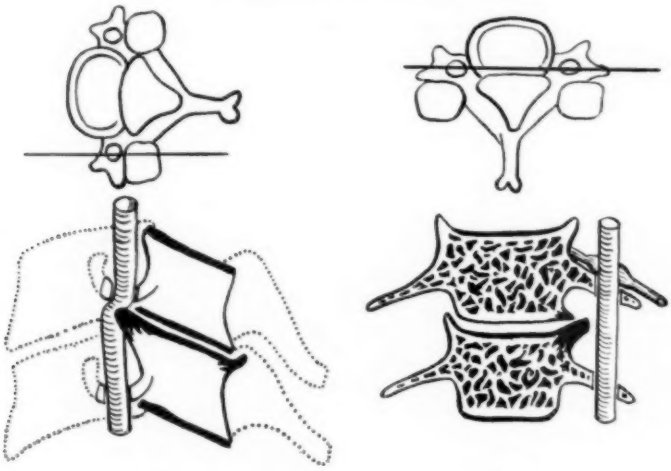
Fig. 15. (a) Wedge-shaped deformation of disk between C III and C IV, with articular processes in subluxation. (b) Film of the foramen showing its contraction by the thickened extremity of the articular process.

Glisson's traction, massage, rest, and paravertebral novocain infiltrations were employed. The symptoms gradually improved.

Slipping of the articular process to below the transverse process was observed in 22 of 40 cases. In 20 of them, anteflexion-traction of the head was followed by the immediate cessation of the subluxation and headache.

a. b.

Fig. 16. (a) Subluxation of the superior articular process of C IV and C V. (b) Reduced; no headache.



a. b.

Fig. 17. (a) Section made through articular and transverse processes. Broadening of the articular process by some mm or subluxation to the same extent and compression of the artery will ensue. (b) Section through the vertebral body and transverse process. The artery is at a greater distance to the unco-vertebral change and is more likely to remain unaffected.

We believe that headache radiating from the top of the skull and the nuchal region as well as the upper cervical sympathetic syndrome described by BARRE-LIEAU, is more frequently produced by pressure exerted on the vertebral artery and nerve by the superior articular process than by other conditions. The unco-vertebral changes do not affect the artery, unless they extend laterally and exceed 3 to 6 mm. This view is supported by the statement of BARTSCHI-ROCHAIX who found that unco-vertebral changes are frequently unaccompanied by clinical symptoms. Apparently, the unco-vertebral changes, in these cases, do not attain the size mentioned, do not extend to the artery, nor protrude lateralwards in front of the site of the artery (Fig. 17b). We therefore differ from BARTSCHI-ROCHAIX who claim (p. 85 of their monograph) "Natürlich kann daneben auch eine spondylarthrotische oder spondylotische Reaktion bestehen. Ob dies der Fall ist oder nicht, spielt praktisch eine nur nebensächliche Rolle . . . die für das Zustandekommen der Migraine cervicale vollkommen irrelevant ist." We are of the opinion that the rôle of the articular processes is decisive.

SUMMARY

The upper articular process of the cervical vertebrae frequently becomes dislocated and compresses the vertebral artery and the accompanying sympathetic nerve against the border of the foramen of the transverse process above. Bilateral or unilateral headaches, as a result of this, may result. These headaches cease while the subluxation is being reduced by anteflexion-traction of the head. A film taken during this manipulation shows that the articular process has been removed from the transverse process. Similarly, inflammatory or degenerative changes in the small joints resulting in widening of the articular process may, by extension below the transverse process, cause contraction or circulatory disturbance of the artery, and consequent headaches.

ZUSAMMENFASSUNG

Der obere Gelenkfortsatz der Halswirbel wird bei der Subluxation eines Gelenkes nach vorn verschoben und drückt die A. vertebralis mit dem sie begleitenden N. symp. vertebrae an den Rand des vom darüber befindlichen Querfortsatz gebildeten Foramens. Hierdurch kann es zu ein- oder beiderseitigen Kopfschmerzen kommen. Kopfschmerzen dieser Art hören nach der unter energischem Zug ausgeführten Anteflexion des Kopfes auf. Diese Manipulation beseitigt auch die Subluxation und eine in diesem Zustand angefertigte Aufnahme zeigt, dass der Querfortsatz vom Gelenkfortsatz entfernt ist. Ähnliche Kopfschmerzen werden auch durch degenerative oder entzündliche Kleingelenkprozesse herbeigeführt, da diese eine Verbreiterung des Gelenkfortsatzes zur Folge haben. Der breite Gelenkfortsatz kann durch Ausdehnung bis unter den Querfortsatz zu einer Verengung der Arterie und Kreislaufstörungen Anlass geben.

RÉSUMÉ

L'apophyse articulaire supérieure des vertèbres cervicales se luxe fréquemment et comprime l'artère vertébrale et le nerf sympathique qui l'accompagne contre le bord du

trou de l'apophyse transverse sus-jacente. Il peut en résulter des céphalées bilatérales ou unilatérales. Ces céphalées cessent quand la subluxation est réduite par antéflexion et traction de la tête. Un cliché pris pendant cette manipulation montre que l'apophyse articulaire a été éloignée de l'apophyse transverse. De même, des altérations inflammatoires ou dégénératives des petites articulations causant un épaississement de l'apophyse articulaire peuvent, en s'étendant au dessous de l'apophyse transverse, donner lieu à un spasme ou à des troubles circulatoires de l'artère vertébrale et à des céphalées qui en résultent.

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FOREIGN BODY GRANULOMAS FOLLOWING HYSTEROSALPINGOGRAPHY WITH A CONTRAST MEDIUM CONTAINING CARBOXYMETHYL CELLULOSE

by

F. Bergman, G. Gorton, O. Norman and *S. Sjöstedt*

Hysterosalpingography has gradually become an essential part of the examination in an increasing proportion of gynecologic disorders. Formerly, the method was used mainly for the demonstration of tubal patency or occlusion, particularly in the investigation of sterility. In recent years hysterosalpingography has found wider use as a diagnostic procedure in the demonstration of uterotubal malformations, submucous myomata, adenomyosis, carcinoma of the uterus and, to a certain extent, genital tuberculosis.

This trend placed new demands on the contrast media for hysterosalpingography. Various agents were used for this purpose, the most popular being Lipiodol. This substance has, however, since fallen into disrepute in many countries because it involves the risk of production of foreign body granuloma (RUBIN 1936 and 1939, BERGIN 1951 and RENDELSTEIN 1953), embolism (ROBINS & SHAPIRA 1931, WILLIAMS 1944, BERGIN 1951) and inflammatory changes in the tubes and uterine mucosa (TITUS et coll. 1937). Since KJELLBERG's investigations (1942), it has been the rule in Sweden to use water-soluble contrast media in place of Lipiodol. A disadvantage of these water-soluble contrast media is, however, that being thin, they often pass through the uterine cavity and tubes fairly quickly and thereby diminish the possibility of detecting the presence of any abnormalities. In addition the amount of the contrast fluid entering the pelvic cavity is sometimes such as to impair the proper interpretation of any changes in the tubes, uterine cavity or

Submitted for publication, 6 September 1954.

cervix. These disadvantages do not attend a more viscous contrast medium such as Lipiodol, which being thicker, does not sweep through the tubes so quickly and thereby gives a more informative filling of the uterus and the tubes. Moreover, the amount of viscous contrast medium necessary for the production of satisfactory hysterograms is smaller. This in turn diminishes the amount passing into the pelvic cavity and thereby the risk of utero-tubal changes being masked by such a spill.

In an attempt to secure the advantages of Lipiodol and of the thin, water-soluble contrast media, without the otherwise inherent disadvantages of these media, a search was made for suitable thickeners for increasing the viscosity of the water-soluble media. The first contrast medium of this type was Visco-Rayopak (RUBIN 1941) in which the thickener consisted of polyvinyl alcohol. According to MORALES & HEIWINKEL (1948) and MARSHAK et coll. (1950), this preparation exerts more than negligible irritation. In order to increase the viscosity MORALES & HEIWINKEL (1948) added carboxymethyl cellulose, CMC, to the water-soluble contrast medium Umbradil (in which 3 : 5-diiodo-4-pyridone-N-acetic acid is the radiopaque substance). CMC is water-soluble and is said not to be toxic (HUEPER 1944, 1945, WERLE 1941, SHELANSKI & CLARK 1948). A number of similar contrast media for hysterosalpingography and bronchography have since become available (*e. g.* Medopaque H, U. S. A.; Dionosil, England; Per-Abrodil BR and HS, Germany; Joduron B and S, Switzerland; Umbradil Viskös B, H and U, Sweden).

At the Roentgendiagnostic Department of the University of Lund, we began to use Umbradil-Viskös H for hysterosalpingography in 1949. Towards the end of 1951, a number of granulomatous formations were seen in the operative specimen of a uterus removed for myoma. No explanation could be offered for the cause of these formations, but our thoughts were gradually directed to the possibility of the contrast medium used for hysterosalpingography performed in the earlier investigation of the case being responsible for the lesions. In order to check this possibility the present study was started.

The purposes of the investigation were 1) to determine whether these granulomas are due to the contrast medium, 2) to assess the frequency of such formations following hysterosalpingography, 3) to estimate how soon after the examination the granulomas develop, 4) to appraise how long they persist, 5) to find an explanation for their situation, and 6) to judge the clinical importance of the growths.

Material

The material consisted of operative specimens from the Department of Obstetrics and Gynecology (19 cases), Radiotherapeutic Department, Gynecological Section (5 cases), Lund, and from the Department of Obstetrics and Gynecology Central Hospital,

Kristianstad (1 case). In all of these cases, the patients had been submitted to hysterosalpingography with a contrast medium containing CMC (Umbradil Viskös H) before operation.

In 18 cases (Nos. 1—18 in Table 1) a large number of sections from each specimen were carefully studied.

In addition, histologic sections from 46 patients who had previously undergone hysterosalpingography with the same contrast medium were re-examined. In these cases, only a few sections were available, the operative specimens having long been rejected. The retrospective part of the investigation therefore was necessarily limited to a re-examination of the sections available.

The investigation was also extended to include a few animal experiments. Umbradil Viskös H was injected intramuscularly into a small number of mice which were killed at varying intervals and examined. The purpose of these animal experiments was to obtain vital tissue which had contained CMC for different periods.

Staining. After the specimen had been fixed in formalin and embedded in paraffin, sections were cut and stained in haematoxylin-eosin, toluidine blue, mucicarmine and periodic acid by the method of Hotchkiss & McManus.

Table 1

Summary of case reports

(Blank space = not examined)

No.	Age	Hysterosalpingography Contrast medium in			Granulomas observed in			Interval in days between hysterosalpingography and operation	Diagnosis
	in years	venous reflux	tube	abd. cave	uterus	tube	ovary		
1	50	—	—	—	—	—	—	5	Myoma and adenomyosis interna
2	47	—	+	+	—	—	+	1,276	Adenomyosis interna
3	59	+	—	—	+	—	—	114	Myoma
4	33	+	+	+			+	118	Normal ovary
5	49	+	—	—	+	—	—	4	Myoma and adenomyosis interna
6	54	+	+	+	—	—	+	143 & 164	Carcinoma of the corpus uteri
7	60	—	+	+	—	—	+	14 & 115	Carcinoma of the corpus uteri
8	43	+	—	—	+			7	Myoma and adenomyosis interna
9	44	—	—	—	—			6	Myoma and adenomyosis interna
10	51	+	—	—	+	—	—	6	Myoma
11	38	—	+	—		+		7	Chron. salpingitis
12	48	—	—	—	—	—	+	5	Myoma
13	37	—	+	+	—	+	—	5	Myoma
14	57	—	+	+	+[1]	—	—	7	Myoma
15	40	—	+	+	+[1]	—	+	25	Carcinoma of the corpus uteri
16	64	+	—	—	+	—	—	3	Clim. metrorrhagia
17	32	—	+	+	—		+	237	Myoma
18	48	+	—	—	+	—	—	25	Carcinoma of the corpus uteri
19	40	—	+	+	+[1]			2	Myoma
20	41	—	+	+			+	7	Bilat. ovarian endometriosis
21	54	—	+	+			+	1	Carcinoma of the corpus uteri
22	54	—	—	—	+			10	Myoma
23	42	+	+	+	+			4	Metropathia haemorr. cystica
24	51	—	—	—	+			3	Adenomyosis interna
25	49	—	+	+			+	7 & 209	Myoma

[1] Changes only on the serosa surface.

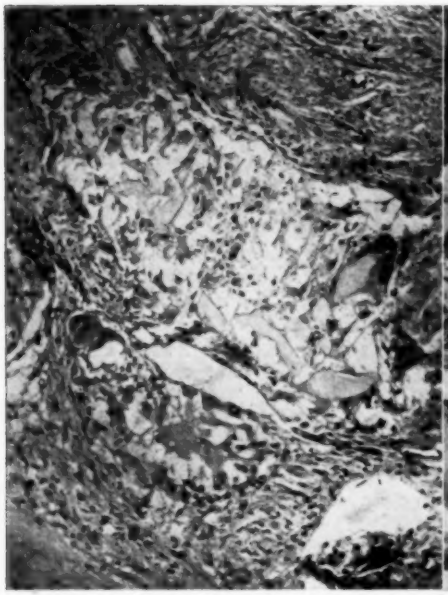

Fig. 1. (Case 8) Granuloma situated in the myometrium and built up of hyaline substance surrounded by histiocytes and giant cells.

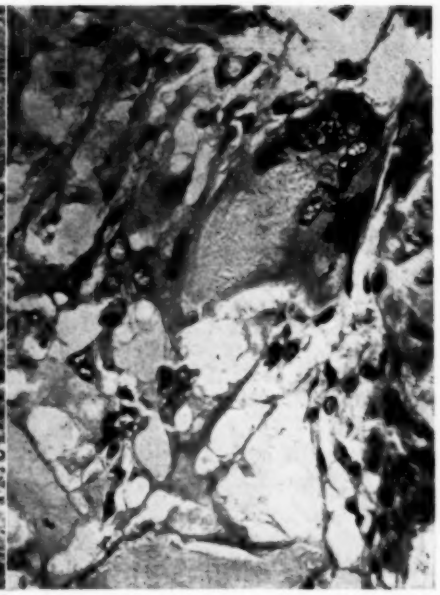

Fig. 2. (Enlargement of part of Fig. 1) Giant cells containing hyaline foreign bodies. Histiocytes are seen in the surroundings.

Results

The results of the examination are summarised in Table 1, which gives data on the roentgen findings of interest, on the parts examined histologically, on the granuloma found, the interval between hysterosalpingography and the operation and the diagnoses established. Of the 18 cases studied (cases 1—18) granulomas were seen in 16. Of the 46 cases in which histologic sections were re-examined, granulomas were demonstrated in 7 (cases 19—25).

The lesions observed — granulomas — in the genital tract were essentially of one and the same type, the histologic appearance of which was characterised mainly by a foreign body substance resembling hyaline. When stained with haematoxylin-eosin it showed basophilia. It closely resembled mucus, but did not colour with ordinary mucous stains (mucicarmine and periodic acid according to Hotchkiss & McManus). On the other hand, the substance showed pronounced metachromasia when stained with toluidine blue and assumed a red-violet colour. Tinctorially, the substance behaved exactly like CMC.

Fig. 3.

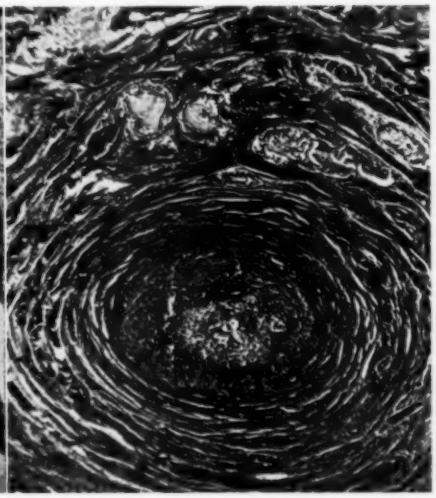

Fig. 4.

Fig. 3. (Case 13) Mucus-like masses surrounded by abundant polymorphonuclear leucocytes in the lumen of the tube.

Fig. 4. (Case 11) The tubal lumen is completely filled with granulation tissue surrounding hyaline masses. A number of cavities filled with hyaline masses surrounded by histiocytes are apparent in the musculature. Epithelial rests are seen in some of the cavities.

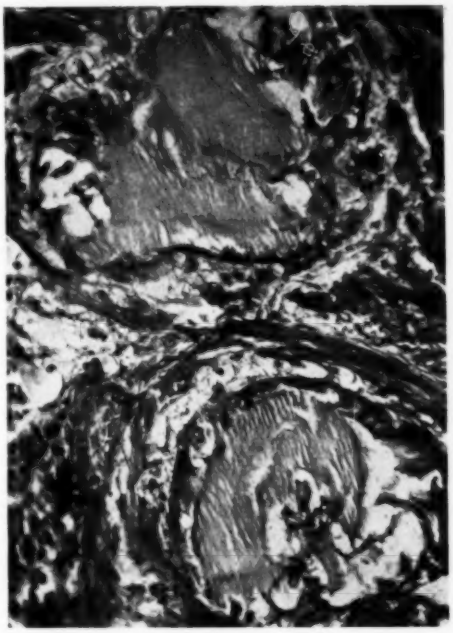

Fig. 5.

Fig. 5. Enlargement of part of Fig. 4.

Fig. 6. (Case 15) Widespread foreign body granuiomas on the surface of the uterus.

Fig. 7. (Case 6) Granuloma on the surface of the ovary. Hyaline masses surrounded by giant cells and histiocytes are seen in the middle. Fibrous tissue is apparent out in the periphery. In the lower part the ovarian surface and narrow spaces lined with mesothelium are present.

More or less marked inflammatory changes were observed around the spots of viscous contrast medium. In sections representing the acute stage (the first few days after the injection) the picture was dominated by an accumulation of polymorphonuclear leucocytes, while those representing a somewhat later stage were characterised above all by large histiocyte-like, pale-staining cells. These crowded around the particles of contrast medium to form granuloma-like formations. Groups of multinuclear giant cells (Figs. 1 and 2) with particles of the viscous component of the contrast medium in the cytoplasm were not uncommon. In addition to the histiocytes, a moderate admixture of round cells was seen as well as perifocal fibrosis increasing with the interval between the injection and the examination.

Changes were found in the myometrium, tubes and ovaries. The myometrial lesions were the most common and appeared as more or less numerous foci. Sometimes scattered granulomas were observed between the muscle bundles (Fig. 1). In some cases the spots of viscous contrast

medium were encircled by a histiocytic reaction in endothelium-lined spaces, apparently sinusoid vessels in the myometrium. The changes were not infrequently seen close to the myoma, but never within the actual tumor. In cases with adenomyosis, changes were often observed around the abnormally disposed endometrial elements. Sometimes the granulomata were few, though usually numerous.

Tubal changes were seen in only 2 of the 14 cases examined. Early cases showed only contrast medium in the tubal lumen which contained an accumulation of polymorphonuclear leucocytes (Fig. 3). In 1 case (Figs. 4 and 5) numerous granulomas were seen in the muscularis of the tubes. In this case the tubal wall showed endometrial elements, in which were particles of contrast medium surrounded by typical inflammatory changes.

The ovaries often showed changes and these were always superficial. The granulomas, which appeared as gray-yellow nodules, were often visible with the naked eye. In some instances they were closely packed in large confluent formations covering a fair proportion of the ovarian surface. Such granulomas were also seen in other parts of the peritoneal surfaces in the small pelvis. In 1 case widespread granulomas were observed on the surface of the uterus (Fig. 6). These were similar in type to those seen elsewhere. In another case (in which the patient had been operated on the day after hysterosalpingography with contrast medium containing the thickener), the ovarian surface showed hyaline masses surrounded by polymorphonuclear leucocytes. Less recent changes showed a pronounced histiocytic reaction, and in fairly long-standing cases the surfaces of the ovaries presented fibrous patches in the middle of which were spots of viscous contrast medium (Fig. 7). These superficial ovarian changes were not related to any intra-ovarian lesions, for they were also seen in otherwise healthy ovaries.

Discussion

Viscous contrast media containing CMC were not only studied before they were accepted for clinical use, but have also since been the subject of both experimental and clinical investigation.

Morales & Heiwinkel (1948) for example, reported that the intra-arterial injection of such media into calves and the intraperitoneal, intrapleural and subpericardial injection into rabbits was not followed by any demonstrable irritation. They did not state the interval between the injection and the examination of the tissues. On the other hand, in bronchographic studies in rabbits and rats, Hellström & Holmgren (1949) observed a pronounced thickening of the alveolar septa 6 hours after the injection of viscous contrast media. However, these changes passed off within 1 to 2 weeks and, after a further week, the histologic

picture was on the whole normal. WICKE & MARTHEN (1952) injected Joduron B intraperitoneally and extraperitoneally into guinea-pigs. Subsequent examinations, usually at the most 24 hours later, revealed a light, foreign body reaction. Only 2 of the animals were allowed to live for 12 days after the injection. Neither of them showed histologic signs of severe or prolonged irritation. These authors therefore concluded that it was justified to use Joduron clinically. BURGER (1952), on the other hand, found the intraperitoneal injection of such media to cause irritation in the peritoneum, but he did not consider this side-effect severe enough to contra-indicate clinical use of the medium. DIETZ & SCHNEIKART (1953) studied the effect of a large number of preparations containing CMC in rats. Their experiments included some resembling hysterosalpingography, and the animals were examined after a varying period of up to 8 days. As the only side-effects observed were hyperemia and exudation, both of which appeared within a few hours but soon passed off, they concluded that the media could be classed as non-injurious and therefore be used clinically.

Although animal experiments thus argue in general in favour of viscous contrast media being non-injurious, there has still been a divergence of opinion on this point among clinicians. The use of these contrast media for bronchography has received special attention. MORALES & HEIWINKEL (1948) and later MORALES (1949) observed no clinical signs of complications after their use in hysterosalpingography, bronchography, arthrography, mastography and urethrography, for example. FISCHER (1948 and 1950), DE FINE LICHT (1950), SCHULTZ-MÖLLER (1951), LENZI (1952) and DON (1952) recommended the use of viscous media for bronchography. On the other hand, VISCHER (1951) described inflammatory changes in the lungs following bronchography with contrast media containing CMC. ZOLLINGER (1951) criticised VISCHER's conclusion on the grounds that the granuloma described by VISCHER was probably ascribable to an accumulation of mucus in the lungs due to some other morbid process. This criticism was, however, afterwards rejected by WERTHEMANN & VISCHER (1951), who produced convincing evidence that the changes under consideration were really attributable to CMC. They also stressed that these lesions seen after bronchography contra-indicated the use of the substance for hysterosalpingography in the investigation of sterility. DU MESNIL DE ROCHEMONT (1952) emphasized that a search should be made for thickeners less injurious than CMC.

Encouraging results with these media for hysterosalpingography have been presented by MORALES & HEIWINKEL (1948), MORALES (1949), KRANZ (1953), DIETZ & SCHNEIKART (1953) and ROLAND et coll. (1953). These reports are, however, based mainly on the clinical reactions noted during and after the examination and not on histologic studies. It is

true that DIETZ & SCHNEIKART studied a few operative specimens histologically and also reported that of 27 women in whom the medium passed through the tubes at hysterosalpingography, 5 nevertheless afterwards became pregnant. On the basis of a fairly large series, BERGMAN et coll. (1952) reported foreign body granulomas to be frequent in patients who had been submitted to hysterosalpingography with a medium containing CMC and issued a warning against the use of such media for hysterosalpingography. MORALES (1952) was unable to find more than a few instances of foreign body granulomas in a large series of operative specimens. In the present investigation, foreign body granulomas were demonstrated in operative specimens from as many as 16 out of 18 women who had previously been submitted to hysterosalpingography with contrast medium containing CMC.

In view of the above observations, two questions present themselves:

Why was the appearance of these granulomas not detected earlier?

Are these granulomas due to the contrast medium?

As to the first question, it should be mentioned that unless special attention be directed to the possible presence of the granulomas, they are easily missed; they do not occur in the myoma, on which the pathologist probably focuses his main attention, but out in the myometrium, and that their detection is to no small degree dependent on the staining methods used. In this last-mentioned respect toluidine blue is useful; it stains the viscous contrast medium metachromatically red-violet, while the surrounding tissue turns blue. This considerably facilitates the demonstration of the granulomas.

As to the second question whether the granulomas are due to the contrast medium and, if so, to which component, the possibility of the amorphous masses being fat or sebum can immediately be rejected. Neither can they consist of mucus; they do not stain like mucus and thus histochemically do not resemble any type of human mucus.

The following points argue strongly for the CMC in the contrast medium being responsible for the development of the granulomas. 1) Tinctorially, the hyaline substance in the granuloma behaves exactly like CMC. 2) The picture of CMC in animal experiments coincided precisely with that seen in the operative specimens. 3) The changes agreed well with those observed by VISCHER (1951) in the lungs of a patient after bronchography with contrast medium containing CMC. 4) The granulomas are seen only in those tissues with which the contrast medium came into contact. a) Changes occurred in the myometrium only in the event of venous reflux (8 of 9 cases) or adenomyosis interna (case 24). b) The uterine serosa was involved only when the contrast medium had entered the abdominal cavity (3 out of 9 cases). c) Tubal changes were

seen only if the contrast medium had entered the tubes (2 out of 7 cases). d) With but one exception, the ovaries demonstrated changes only when the contrast medium had passed out into the abdominal cavity (9 out of 11 cases). In 1 case (No. 12), in which hysterosalpingography was performed mainly for investigating the corpus, no contrast medium was observed in the abdominal cavity. It is, however, known that contrast medium may flow out into the abdominal cavity after the actual examination. The roentgen examinations were carried out under fluoroscopy and usually lasted about 10 to 20 minutes (cf. 24 hours radiograph after roentgen examination with Lipiodol).

These observations strongly argue in favour of the conclusion that the foreign body granulomas were due to the CMC in the contrast medium.

Other points of relevant interest are the rate of development, persistence and clinical importance of the granulomas. It is apparent from Table 1 that they develop fairly soon after the injection. Within as short a time as 1 to 2 days, polymorphonuclear leucocytes may be seen around the spots of contrast medium, and the longer the fibroma persists the more distinct is the fibrosis. In one of the cases (No. 2), in which the patient was operated on more than three years after hysterosalpingography, a foreign body granuloma was found on the surface of the ovary. CMC was demonstrated in the middle of the growth. In 4 other cases, in which the patients were operated on 3 to 8 months after hysterosalpingography, persistent granulomas were encountered. In 3 of these, in which contrast medium had passed out into the abdominal cavity, the changes were seen on the surface of the ovaries. It thus appears that the changes may persist for a long time, perhaps years, particularly on the surface of the ovary.

The clinical importance of these granulomas is perhaps debatable. At the Department of Obstetrics and Gynecology, hysterosalpingography with viscous contrast media has not been found to be accompanied or followed by such symptoms as pain, fever or peritoneal irritation, to suggest that this contrast medium should be less suitable than others. At the Radiotherapeutic Clinic, with its higher frequency of cancer cases, however, the number of such complications increased after the introduction of contrast medium containing CMC. The complications often made it necessary to treat the patient with antibiotics and postpone radiotherapy. In 2 cases (6 and 15), for instance, the patients were even operated on because of severe pain in the lower part of the abdomen after hysterosalpingography and radiotherapy. In neither did operation reveal any signs of salpingitis, pelviperitonitis, or residual cancer in the uterus or ovaries, and the pathologist was unable to offer any explanation for the severe pain except for the presence of numerous granulomas. As

this increase in the frequency of complications did not appear until the introduction of viscous contrast media, and as this was the only modification made in the examination and treatment, it was decided to revert to the use of thin, water-soluble contrast media containing no CMC. Since then the frequency of complications has been practically nil.

Although clinical experience with contrast medium containing CMC may thus differ from one department to another, it is obvious that the ovarian and tubal changes of the type described cannot simply be dismissed as insignificant. It is beyond doubt that the occurrence of granulomas involving a large proportion of the ovarian surface must impair or even prevent the discharge of the ovum. The risk of such complications must therefore contraindicate the use of contrast medium containing CMC for hysterosalpingography in the investigation of sterility and of women in fertile age. If the patient has passed this age, the development of a granuloma might be of less importance, but even then we prefer contrast media without such side-effects. At any rate, the use of contrast media containing CMC has been abandoned at the University Clinics of Lund.

Conclusions

Hysterosalpingography with contrast media containing CMC was usually (in 16 out of 18 cases) followed by the development of foreign body granulomas in the myometrium, tubes or surface of the ovaries. These granulomas, which were due to CMC, appeared only in those tissues that had been exposed to the action of the contrast medium. Thus, the lesions appeared in the myometrium only in the event of venous reflux or adenomyosis. They were demonstrated in the peritoneum and on the ovaries only when the contrast medium had passed out into the abdominal cavity, and only when the medium entered the tubes were any tubal lesions seen. The granulomas develop rapidly (within 1 to 2 days) and may persist for years, especially when situated on the surface of the ovaries. The clinical importance of these changes is debatable, but it is obvious that contrast media containing CMC should not be used for hysterography in women of fertile age. In women beyond this age, their use might be defensible, but even then other contrast media should preferably be employed.

SUMMARY

Foreign body granulomas were demonstrated in 16 out of 18 patients following hysterosalpingography with a contrast medium containing CMC. The lesions were seen in the uterus in 8, in the tubes in 2 and in the ovaries in 7 cases.

Re-examinations of histologic sections of operative specimens still available from 46 patients who had also been examined with this contrast medium revealed granulomas in the uterus in 4 and in the ovaries in 3.

It is shown that the changes were due to the CMC content of the contrast medium.

ZUSAMMENFASSUNG

Im Anschluss an die Hysterosalpingographie mit einem Kontrastmittel, welches Carboxymethylcellulose (CMC) enthält, wurden bei 16 von 18 Patienten Fremdkörpergranulome festgestellt. Die Veränderungen wurden in 8 Fällen im Uterus beobachtet, in 2 Fällen in den Tuben und in 7 Fällen in den Ovarien.

Die nachträgliche Durchsicht histologischer Schnitte von Operationspräparaten, die noch von 46 Patienten, welche ebenfalls mit diesem Kontrastmittel untersucht worden sind, zugängig waren, zeigten Granulome im Uterus in 4 Fällen und in den Ovarien in 3 Fällen.

Es wird gezeigt, dass die Veränderungen vom CMC-Gehalt des Kontrastmittels hervorgerufen werden.

RÉSUMÉ

Les auteurs ont mis en évidence des granulomes à inclusion de corps étrangers chez 16 malades sur 18 à la suite d'hystérosalpingographie avec un produit de contraste contenant de la carboxyméthylcellulose (CMC). Ils ont trouvé ces lésions au niveau de l'utérus dans 8 cas, des trompes dans 2 cas, et des ovaires dans 7 cas.

Un nouvel examen des coupes histologiques de pièces opératoires de 46 malades qui avaient elles aussi été examinées au moyen de ce produit de contraste a montré des granulomes au niveau de l'utérus dans 4 cas, et des ovaires dans 3 cas.

Les auteurs prouvent que ces lésions sont dues à la CMC contenue dans le produit de contraste.

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ROTATION TOMOGRAPHY AT SMALL ANGLES

by

Knut Lindblom

The many types of apparatus for tomography with linear, circular and spiral movements, which have been constructed, have possessed two factors in common — the relatively great angle of movement and long exposure time.

It was pointed out by DE ABREU, VALLEBONA, et al. in dealing with the principles of tomography that the thickness of section is inversely proportional to the angle of movement. The validity of this rule was usually demonstrated in the tomography of small metal objects with ideal contrast and spherical shape and consequently with well-defined outlines.

Certain facts seem to have been forgotten. The structure ofthe human body possesses little ideal contrast and but small movements will blur this out in the film. Furthermore, the large angles of movement will cause distortion of the structures as shown in Diagr. 1. The shadow of the ring A is elongated from S to S_2 by moving the focus from point F to F_2 whereas the elongation S to S_1, representing a small angle of movement, is negligible.

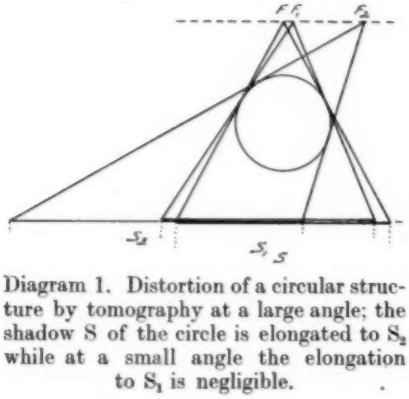

Diagram 1. Distortion of a circular structure by tomography at a large angle; the shadow S of the circle is elongated to S_2 while at a small angle the elongation to S_1 is negligible.

The definition of contours in tomography is illustrated in Fig. 1. A ping-pong ball was tomographed with 10 and 40 degrees of movement. High definition was obtained in the former case and in the latter the zone of blurring was 2 mm.

Submitted for publication, 23 June 1954.

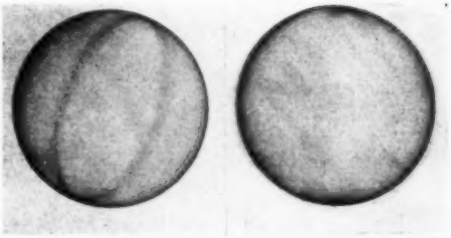

Fig. 1. Tomograms of a ping-pong ball; to the left, high definition with circular tomography at 9 degrees; to the right, blurring of contours with tomography at 45 degrees.

Blurring depends upon the angle of movement as well as upon the size of the structure. The blurring should not be more than the lack of definition of the intensifying screens, that is about 0.4 mm. For spherical and cylindrical structures the blurring may be expressed according to the formula $\frac{S + 0.4}{S}$, where S equals the 'shadow of the structure'.

The correlation between this ratio and the angle of movement is illustrated in Diagram 2. If the value of the ratio is plotted on the abscissa the angle of movement permissible may be read off on the ordinate. It is seen that the shadow of a spherical structure, 20 mm in diameter, will be noticeably blurred at an angle of more than 7 degrees. The corresponding angles for 10 and 5 mm are 9 and 17 degrees respectively.

It is true of all ordinary tomograms that nothing is really well-defined. Central structures with moderate definition are seen against a background of marked unsharpness. Using small angles of movement with consequently less distortion, the central structures will appear with a higher definition against a background of a moderate degree of blurring. The eye will notice the well-defined structures and the unsharp ones will drop out.

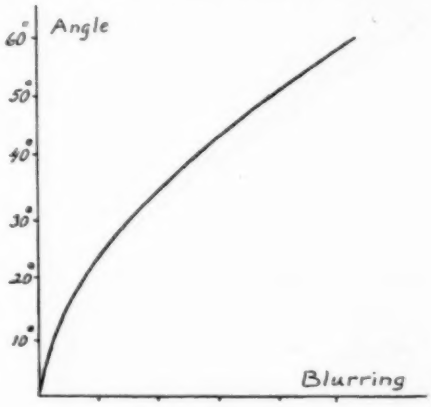

Diagram 2. Diagrammatic expression of $\frac{S + 0.4}{S}$.

The invalidity of the rule of inverse proportion between thickness of section and angle of mo-

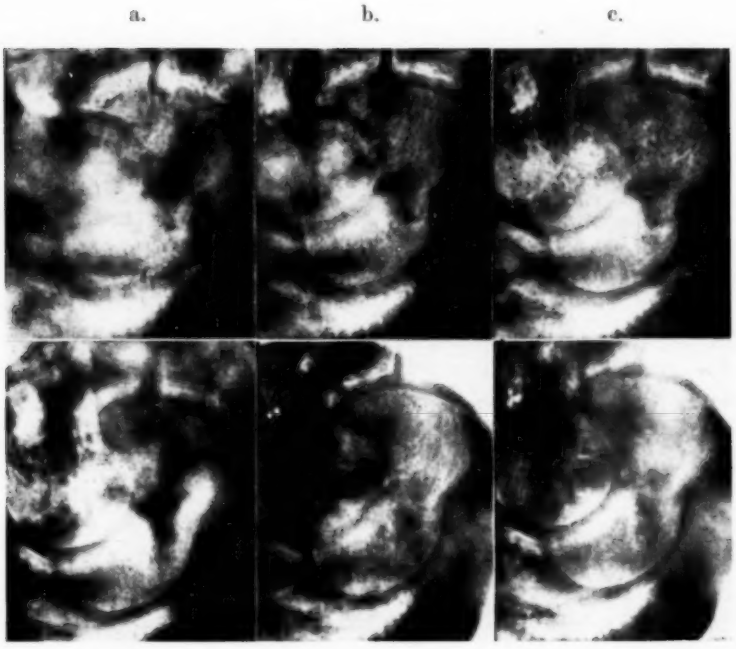

Fig. 2. Rotation tomograms at 9 degrees of navicular fracture in plaster. Distance between sections 2.5 mm. a—d: Not healed. e—f: Six weeks later with bone formation visible at site of fracture.

vement is demonstrated by the tomograms in Fig. 2. This shows a navicular fracture during and after healing, tomographed at sections of 2.5 mm. The angle of movement is 9 degrees. The different appearance of the sections in spite of the small angle will be noted.

The film in Fig. 2 was obtained with the apparatus for rotation tomography at small angles. The apparatus is described and illustrated in another paper (2) and was used for the study of the lungs, bones and soft tissues. The spongeous structure of bones was well-defined. In the temporal bones the spongiosa could be distinguished from small mastoid cells and details such as the incus and the stapes were visualized. The healing of fractures was studied through plaster, the tomograms of navicular fractures being of special value.

The lung structures were markedly well-defined by reason of the exposure time being as short as 0.1 second. In determining the extent

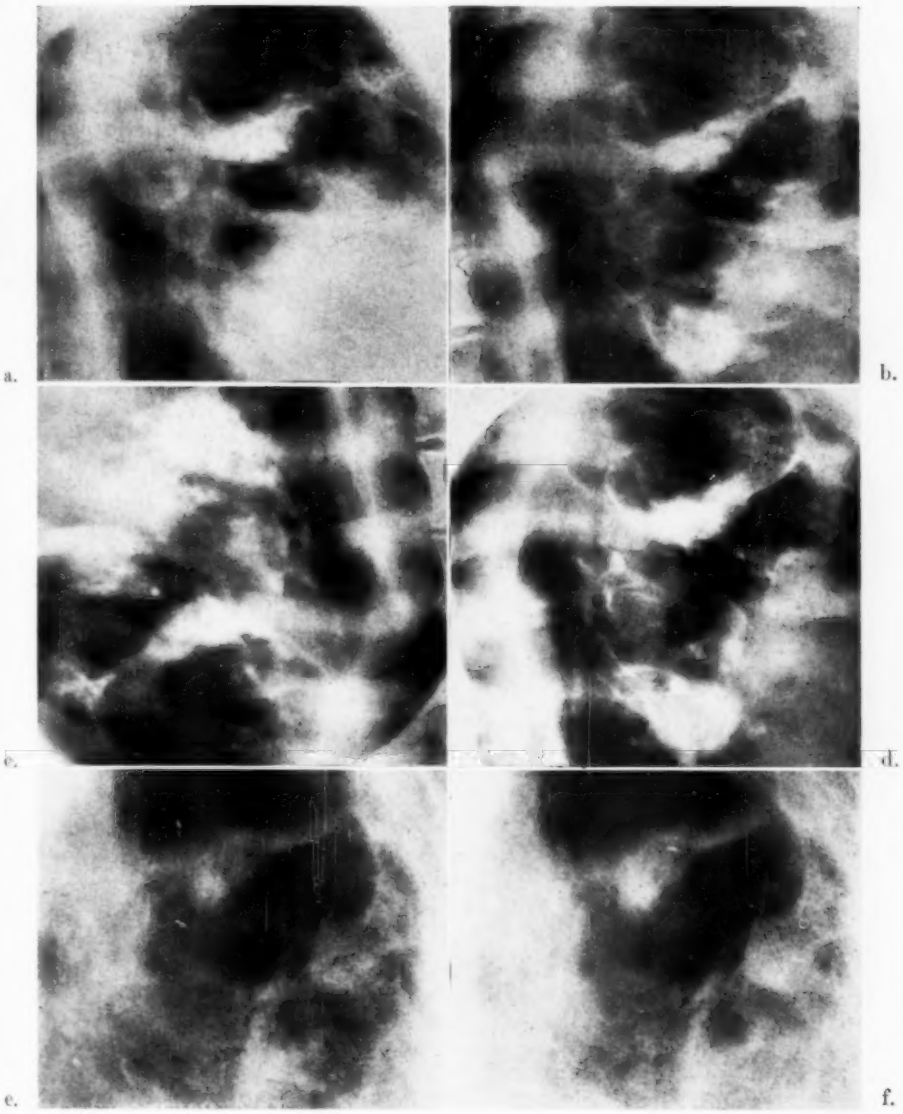

Fig. 3. Tomograms of lung with tuberculous atelectasis. Distance between sections 1 cm. a—d were taken with the apparatus for rotation tomography at 9 degrees; e—f with an ordinary apparatus for tomography. Note the differences in definition.

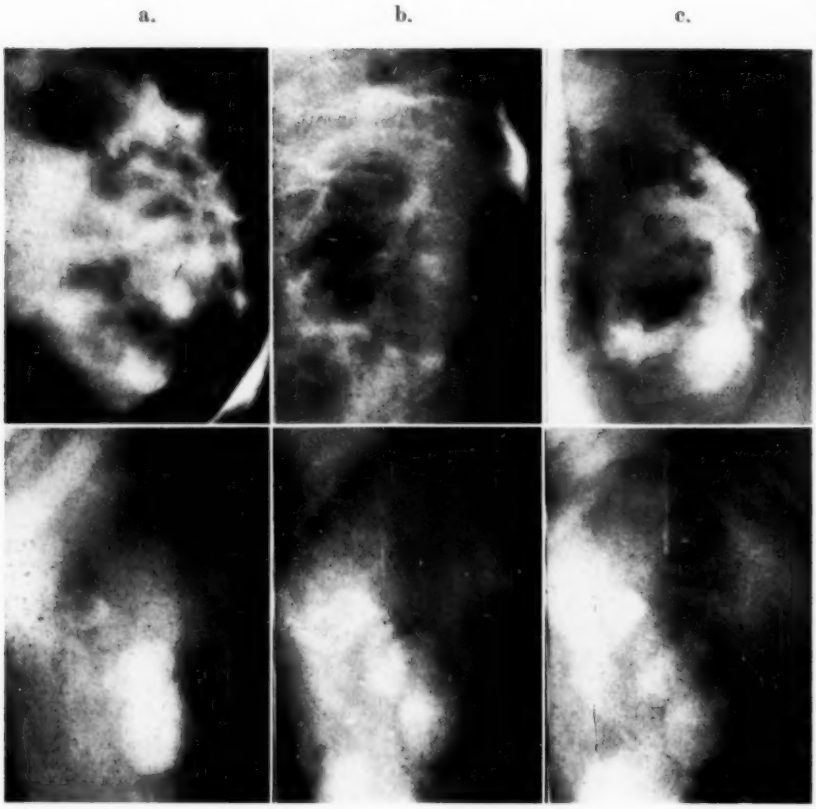

Fig. 4. Rotation tomograms of three mammary glands (a—c) and of axillary metastases (d—f) in a case of mammary carcinoma. a. Lactating breast. b. Normal breast at menopause. c. Widespread carcinoma of breast. d—f. Three sections at 1 cm distance of the axillary structures.

of diseased segments of the lungs, the tracing of the vessels from the hila out to the periphery, made possible by the high definition, proved to be of great value. Comparative tomograms of a lung obtained with this apparatus and by the usual method are illustrated in Fig. 3.

The study of soft tissue structures was most interesting. Mammary glands were examined under ordinary conditions and during lactation as well as in cases of tumours in many of which metastases were seen (Fig. 4). It was possible to visualize parts of the pancreas in its surrounding fat. The infiltration of malignant tumours could be seen in adjacent

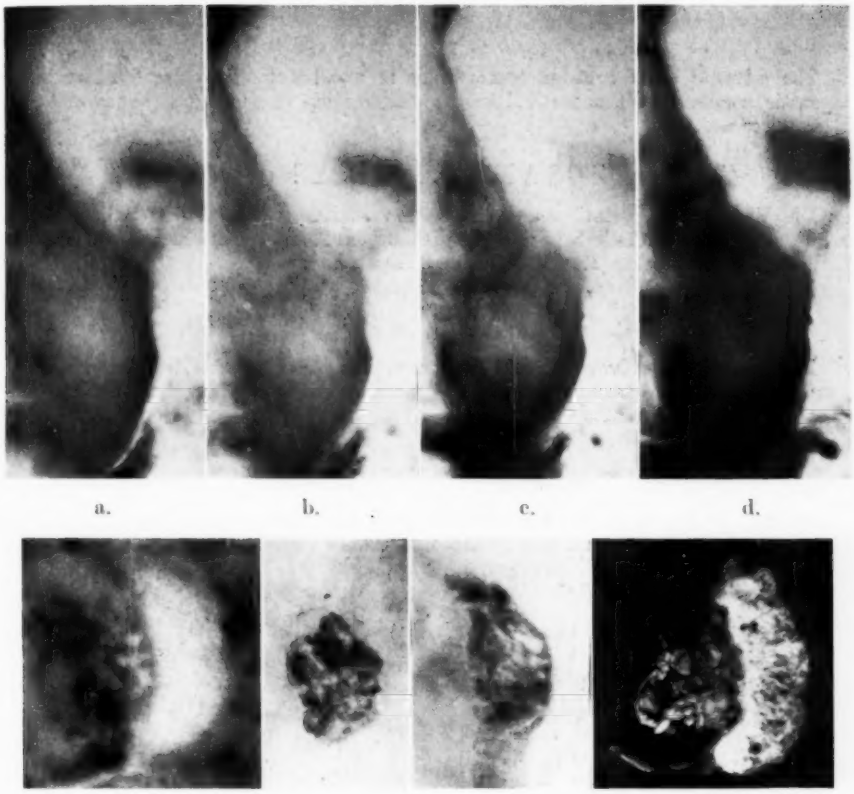

Fig. 5. Case of carcinoma of stomach just below cardia with regional lymph node metastases in the lesser omentum. Before operation rotation tomography demonstrated gradual thickening of stomach wall at the site of the tumour (a—c) and projection of masses from the tumour into lesser omentum (d). e. Tomography of operation specimen in water verified presence of nodular masses in the lesser omentum close to the tumour base. f—g. Similar structures seen in ordinary roentgenograms. h. Photograph of sections through tumour and lesser omentum.

fatty tissue (Fig. 5), the high definition of non-infiltrating tumours being a prominent feature.

The dilated renal pelvis in case of obstruction by ureteric calculi was defined. In order to demonstrate the details of these tomograms, they were copied onto very hard films, the contrast thus being increased to its maximum. It is hoped that the image amplifier, perhaps combined with television, will widen the possibilities for this kind of examination.

SUMMARY

The advantages of rotation tomography at small angles are described and the diagnostic results with this method in the examination of the lungs, bones and soft tissues discussed.

ZUSAMMENFASSUNG

Die Vorteile der Rotationstomographie mit kleinen Winkeln werden beschrieben und die mit dieser Methode bei der Untersuchung der Lungen, Knochen und Weichteile erhaltenen diagnostischen Resultate werden besprochen.

RÉSUMÉ

L'auteur décrit les avantages de la tomographie rotatoire sous de petits angles et examine les résultats diagnostiques obtenus par cette méthode dans l'examen des poumons, des os et des parties molles.

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ENCEPHALOGRAPHY IN BRAIN TUMOURS

A review of 104 cases

by

Giovanni Ruggiero, Marcel David and *Jean Talairach*

Fractional encephalography using the technique described by LINDGREN (4) has been carried out in cases of brain tumour in the neuroradiodiagnostic laboratory of the Neurosurgical Centre of St. Anne's Hospital for nearly 2 years. In a previous paper (2) in which the authors compared the results of 40 encephalographies and 30 ventriculographies performed in cases of brain tumour, it was shown that the former examination cannot be considered more dangerous than the latter. Further experience has confirmed this statement, and encephalography is now the first and often the only pneumographic examination performed in nearly all our cases. The problem of the danger of encephalography and its reliability in comparison with ventriculography will, therefore, not be discussed in this paper which will deal only with brain tumours.

Material

The material consists of 104 cases of brain tumour in which fractional encephalography has been carried out. Seventy-six cases have been verified anatomically by operation or autopsy followed by histologic examination. Twenty-eight cases were not verified anatomically but the presence of a tumour was evident from the clinical and radiologic examinations. The material is schematically listed in Table I.

In the cases of Group A 1 the lesion was exactly localized by encephalography which indicated also its extra- or intracerebral situation but did not specify the histologic type. In tumours of the posterior fossa and of the base of the skull, the diagnosis of the extra- or intracerebral situation is easier and often suggests the pathology of the lesion. In our

Submitted for publication, 27 August 1954.

Table I

Results of lumbar encephalography in 104 cases of brain tumour

	Verified	%	Non-verified	%
A. *Diagnostic*				
1. Site and situation in relation to the brain (extra- or intracerebral)	29	38.15	14	50
2. Site and situation in relation to the brain probable	12	15.75	4	14.28
3. Site	23	30.26	5	17.85
4. Site uncertain but probable	6	7.89	5	17.85
	70	92.10	28	
B. *Non diagnostic*				
1. Technical error	1			
2. Error of diagnosis with consequences for the patient	2			
3. Error of diagnosis without consequences for the patient	1			
4. Uncomplete diagnosis without consequences for the patient	2			
	76		28	

series, however, the pathology of the tumour was not infrequently suspected even in cases of hemisphere tumours, but we have had not enough material to draw reliable statistic conclusions.

In Group A 2, the extra- or intracerebral situation of the lesion was suggested. It was, however, always confirmed by operation or other radiologic examinations.

In Group A 3, a diagnosis of the extra- or intracerebral situation could not be made by encephalography and another radiologic examination was necessary. In cases of cerebellar tumours, localization to the posterior part of the posterior fossa was considered satisfactory. In a certain number of these cases the side was also indicated, but, here too, we have not enough cases for statistic purposes.

In Group A 4, the site of the lesion was indicated as probable only. In 3 out of the 6 verified cases, other radiologic examinations were performed which confirmed the encephalographic diagnosis. In the remaining 3 cases, an operation was carried out solely on the basis of the encephalographic findings and the diagnosis proved correct in each case.

Re-examination of the roentgenograms of this group shows that a more precise diagnosis might certainly have been made in 3 cases. This fact, however, has not been taken into consideration since the main purpose of our study was to find out the actual contribution of encephalography to the diagnosis of brain tumours in our hospital.

Discussion

We wish to point out that encephalography has been useful in the diagnosis in 92.1 % (70) of the verified cases (76). It is also very important to note that Group A 1 (diagnosis of the site and situation of the lesion) includes almost half of the verified cases. If one considers the whole material, *i. e.* including the cases non-verified, Group A 1 represents 61.8 % (43 cases) of all the cases in which encephalography was sufficient to make a diagnosis. This higher percentage is probably due to the fact that the majority of 10 non-verified cases are represented by tumours which, following encephalography, were considered inoperable.

In 6 cases, the diagnosis was not made by encephalography.

In 1 case, there was probably a technical error as the air entered the subdural space after a rather difficult lumbar puncture.

In 3 cases, the diagnosis was erroneous; in 1 of these, a cystic tumour in the third ventricle had produced occlusion of the aqueduct and cerebellar oedema with herniation of the tonsils. The diagnosis of a tumour of the cerebellum led to an exploration of the posterior fossa followed by death. The second case was a pontine tumour growing towards the right cerebello-pontine angle. Encephalograms were erroneously regarded as suggestive of an extracerebral lesion in this region, and the patient died following a negative surgical exploration. In the third case, of a young man suffering from impairment of vision without definite changes in the visual field, the error was of no consequence to the patient. Encephalography had led to the diagnosis of opto-chiasmal arachnoiditis, but operation disclosed a very small, almost exclusively intrasellar, pituitary adenoma. The roentgenographic appearances of the sella turcica were normal.

In the last two cases, the diagnosis was incomplete but there were no untoward consequences. In one of these, operation was contra-indicated by the diagnosis of a deep intracerebral expanding lesion in the left temporal lobe, probably invading the basal ganglia. The patient died some time afterwards. Autopsy disclosed a temporal metastasis which had not invaded the basal nuclei, and several other nodular metastases scattered over the brain which was very oedematous. In the other case, encephalography showed an inoperable pontine tumour. Autopsy revealed that the tumour was infiltrating, not only the pons, but also the cerebral peduncles as far as the third ventricle.

One criticism which is often made of encephalography is that cases in which no filling of the ventricular system is obtained are not unusual. According to this objection, such a failure could be due to technical errors or to obstruction — either pathologic or resulting from anatomic

abnormalities — of the foramina between the great cistern and the fourth ventricle. In our opinion, the first occurrence has to be regarded as exceptional if the examination is performed by an experienced roentgenologist. In only one case in the present series was a technical error probable. Congenital absence of the foramina of Luschka and Magendie is very rare.

A pathologic obstruction is, on the contrary, not infrequent. In the present series, there are 20 cases in which no filling of the ventricular system could be obtained. If we exclude the case already mentioned of a probable technical error, 19 cases, *i. e.*, 18.26 % remain. Sixteen of these 19 cases were tumours of the cerebellum; one was a meningioma occupying almost the whole right ventricle, with considerable cerebral oedema, and one a tumour of the brain stem which had obstructed the aqueduct and caused raised pressure in the posterior fossa. In a series of 195 cases of brain tumours examined by encephalography in the Roentgen Department of Serafimerlasarettet in Stockholm, FALK (3) found 24 cases, *i. e.* 12.35 %, in which no filling of the ventricular system had been obtained. In both his cases and our own, the ventricular system could not be visualized in certain tumours of the posterior fossa (especially the posterior part of the posterior fossa). We feel that the higher percentage of failure to fill in our series was probably due to the fact that in our Department encephalography is performed in almost all cases of posterior fossa tumour in which ventriculography has been almost completely abandoned, at least as a first examination (5). As a matter of fact, in FALK's material there are 37 tumours of the posterior fossa among the 195 cases, *i. e.* 18.9 %, while in our series (104 cases) there are 26 (24 confined to the posterior fossa and 2 invading also the middle fossa), *i. e.* 25 %.

In a further 8 cases we did not obtain satisfactory filling of the ventricular system. They were:

1) The cystic tumour of the third ventricle included in Group B 2, already mentioned.

2) A hemispheric glioma invading the corpus callosum included in Group A 4.

3) A frontal bilateral tumour invading the septum pellucidum and the corpus callosum included in Group A 4.

4) A meningioma of the lesser wing of the sphenoid included in Group A 3.

5) A non-verified case, probably a deep infiltrating tumour obstructing the foramen of Monro included in Group A 4.

6) and 7) Two tumours of the brain stem included in Groups A 3 and A 2 respectively.

8) A non-verified case of a calcified, suprasellar, probably intracerebral, tumour invading the central structures, which is included in Group A 4.

Cases 1, 2, 3, 4 and 6 have been verified anatomically. In Case 3, the lesion was clearly shown by ventriculography. In Case 5, the patient refused ventriculography. In Case 7, ventriculography confirmed the encephalographic diagnosis. In Case 8, the patient refused operation. Severe papilloedema was present in all these cases.

Adding the cases of non-filling to the cases of only incomplete filling, we have a total of 27 cases (excluding the one case of technical error) in which visualization of the ventricular system was unsatisfactory. In cases of tumour of the posterior fossa the study of the cisterns is generally sufficient to indicate the site of the lesion, while this does not apply, however, in cases of supratentorial tumour, especially the hemispheric varieties. As a matter of fact, tumours of the brain stem may in certain cases be localized (RUGGIERO, 6), even if the aqueduct is not patent. A detailed discussion of this diagnostic problem, would be, however, outside the purposes of this paper.

Conclusions

An evaluation of the diagnostic value of fractional encephalography in cases of brain tumours has shown us the great value of this technique. It is now the pneumographic examination of choice in our clinic. Encephalography is naturally not sufficient in all cases and ventriculography is still required when poor filling of the ventricular system by the lumbar route does not permit the localization of the tumour. This occurs mainly in tumours causing obstruction of the foramen of Monro or the aqueduct either by direct compression or as a result of cerebral oedema. It should be realized, however, that at times, in the presence of severe cerebral oedema (especially in cases of meningioma), direct injection into the ventricles is possible only if the contrast medium is introduced under relatively high pressure. Such a procedure is necessary in order to fill ventricles which 'refuse air' and may be dangerous (2).

SUMMARY

The authors analyse the results of fractional encephalography in 104 cases of brain tumour, in the diagnosis of 92.1 % of which it was found to be useful. The authors consider fractional encephalography as the pneumographic examination of choice in this condition.

ZUSAMMENFASSUNG

Die Verfasser analysieren die Ergebnisse der fraktionierten Enzephalographie, welche in 104 Fällen mit Hirntumoren benutzt wurde und die sich in 92.1 % der Fälle

für die Diagnosestellung als nützlich erwies. Die Verfasser sind der Ansicht, dass die fraktionierte Enzephalographie bei diesen Zuständen die pneumographische Untersuchungsmethode der Wahl ist.

RÉSUMÉ

Les auteurs analysent les résultats de l'encéphalographie fractionnée dans 104 cas de tumeurs cérébrales, où elle s'est montrée utile au diagnostic dans 92.1 % des cas. Les auteurs considèrent que l'encéphalographie fractionnée est l'examen pneumographique de choix dans ces affections.

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RADIUM AND THORIUM X IN SOME POTABLE WATERS

by

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A number of radium analyses have been made in order to obtain data on natural levels of radioactivity and to help locate potable water supplies having an unusually high radium content as part of a current research program on the toxicity of radium. Several findings of general interest are described in this paper. These may be summarized as follows:

1. The concentration of radium in surface water or shallow wells in the Chicago area is low — less than 0.1 $\mu\mu$c per liter.

2. Water from wells which penetrate into the Galesville formation at a depth of about 1,500 feet or more near Chicago is found to contain from 3 to 8 $\mu\mu$c of Ra^{226} per liter and about the same amount of ThX (3.64—d Ra^{224}). This is believed to be the highest authenticated concentration of radium found to date for any drinking water in the United States.

3. Practically none of the immediate parent of ThX, 1.90—y RdTh, is present in the deep well waters, so the ThX decays after sampling.

4. Drinking water from Frankfurt am Main, Germany, was found to contain less than 0.3 $\mu\mu$c Ra per liter as compared to more than 300 $\mu\mu$c per liter previously reported (8).

Much higher values for the radium content of some spring and mine waters have been reported (10, 7). However, it is recognized that some of the earlier values reported as "radium" were in reality for radon, the activity of which is often several orders of magnitude greater than that of radium in the same water sample. An extreme case of the disparity of radium and radon concentrations in a single water source was reported by KURODA and YOKOYAMA who found a Masutomi spring (designated as A49) in Japan to contain 1.33×10^6 $\mu\mu$c Rn per liter

Submitted for publication, 28 April 1954.

and only 8 $\mu\mu$c Ra per liter (9). The highest radium content reported by KURODA and YOKOYAMA was 76 $\mu\mu$c per liter for Masutomi Spring A5.

The radium content of public water supplies is usually much lower. The highest concentration HURSH (5) found recently in a large number of samples of drinking water from the United States was less than 2 $\mu\mu$c Ra per liter. Values of 190 to 480 $\times 10^{-12}$ grams Ra per liter for the drinking water of Barcelona, Spain, were given by LOVE who did not distinguish between radon and radium in his review paper (10). However, CANALS CRAMP (3) actually had reported his findings on the Barcelona water as radon, and stated that the radium content was too low to be measured with his apparatus.

The necessity of distinguishing between ThX and long lived Ra^{226} in analyses for Ra has received little attention, because most analyses for radium are done by collecting radon, and the presence of small amounts of ThX would have a negligible effect on the results. If the ratio of ThX to Ra^{226} were high, or if radium analyses were made by isolation and measurement of radium then an appreciable error could be made in reporting results as Ra^{226}. The following values (in $\mu\mu$c per liter) reported (9) for Masutomi Spring B7 illustrate a situation in which analytical techniques must clearly distinguish between the radioactive nuclides associated with "radium":

$$Ra^{226} = 31,\ ThX = 320,\ Rn = 2.3 \times 10^3.$$

Analytical Procedures. The chemical procedure used to isolate radium was essentially that developed by AMES and co-workers (1) and RUSSELL, LESKO and SCHUBERT (12). The sample (usually 1 liter) of water was made 0.1 M in HNO_3, evaporated to dryness, and baked to eliminate excess acid. The residue was taken up with 0.1 M HNO_3 and transferred to a 50 ml centrifuge tube. If any insoluble matter remained it was centrifuged off and the clear supernatant retained. A volume reduction step was made by precipitating $PbSO_4$ which carried radium from the solution. After centrifuging, the precipitate was dissolved in a mixture containing six parts concentrated HCl and one part ethyl ether. Then 4.0 mg Ba^{++} carrier was added to precipitate $BaCl_2$ which carried down the radium. After centrifuging, the precipitate was dissolved with a few drops of 0.1 M HNO_3 and the solution transferred to a platinum plate and evaporated to dryness after adding 4 drops 0.5 M H_2SO_4 to form an adherent precipitate of $BaSO_4$. After flaming, the plate was ready for counting.

The activity was measured by counting alpha particles in a windowless proportional counter which had a background of about 0.05 counts per minute (cpm). The disintegrations per minute (dpm) were calculated from the formula:

$$\text{dpm} = \frac{\text{cpm}}{\text{geometry} \times \text{backscatter} \times \text{self-absorption} \times \text{recovery}}$$

The combined geometry and backscattering factors were equal to 0.52. By comparing the counting rate of standard radium samples with Ba carrier added and with no carrier added, the self-absorption factor (for 7 mg $BaSO_4$ distributed over 5 cm^2) was experimentally found to be 0.89. In addition, a recovery factor of 0.96 with a standard deviation

of 5 percent was found by analysis of aliquots of a solution of radium standardized by the Bureau of Standards. Since 1.00 $\mu\mu$c of activity is equal to 2.22 dpm, 1.00 cpm in our apparatus was taken as equivalent to 1.00 $\mu\mu$c Ra for the analysis.

Ra^{226} is followed by 3 alpha-active descendants which are retained in the $BaSO_4$ as they grow in. Accordingly, the counting rates observed had to be corrected to the true radium activity by use of the growth factor for Ra^{226}, R, calculated as follows:

$$R = 1 + 3\,(1 - e^{-0.00755\,t}), \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

where the decay constant for Rn^{222} is 0.00755 hr^{-1} and t is the number of hours after isolation of radium. Furthermore, as will be shown later, ThX was also present in many of the samples. In this case 54.5—s Tn and 0.16—s ThA grew in so rapidly that three alpha disintegrations were obtained for every disintegration of ThX when counting was started. Another alpha-emitting descendant, ThC, grows in more slowly so that the overall growth and decay factor for ThX, X, was as follows when t was greater than 0.1 hr:

$$X = 4.15\,e^{-0.00793\,t} - 1.26\,e^{-0.0654\,t} + 0.11\,e^{-0.688\,t} \quad \ldots\ldots\ldots\ldots\ldots \quad (2)$$

where the decay constants for ThX, ThB, and ThC are 0.00793 hr^{-1}, 0.0654 hr^{-1}, and 0.688 hr^{-1}, respectively.

When both Ra^{226} and ThX were present the amounts of each were calculated by counting the sample twice: once immediately after preparation of the sample and again after a period of a week or more. The equations used are as follows:

$$C_0^{Ra} = \frac{C_2X_1 - C_1X_2}{R_2X_1 - R_1X_2} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (3)$$

$$C_0^{X} = \frac{C_1R_2 - C_2R_1}{R_2X_1 - R_1X_2} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (4)$$

where C_0^{Ra} and C_0^{X} are the true counting rates for Ra^{226} and ThX, respectively, at the time radium was isolated, C_1 and C_2 are the first and second counting rates obtained, and R and X are factors taken from equations 1 and 2 for the times after isolation of radium at which C_1 and C_2 were obtained. In practice, the samples were counted at least three times in order to be sure that the observed growth or decay corresponded to that of Ra^{226} and ThX alone.

Radium Content of Water in the Chicago Area. Samples of drinking water were obtained from communities in the vicinity of the Du Page County site of the Argonne National Laboratory, twenty miles southwest of Chicago. During preliminary studies on some of these samples, the ThX isotope of radium was detected by a study of the growth curve of the alpha activity of the isolated radium. Figure 1 illustrates the growth curves obtained when separate portions of a sample of untreated water from Joliet, Illinois were analyzed 1, 7, 9, 20, and 26 days after the sample was collected. The first count of each succeeding portion was lower than that of the previous portion and the growth for the later portions corresponded more closely to the theoretical for Ra^{226}. These data were interpreted as a result of a mixture of Ra^{226} and ThX in which ThX was decaying because it was not being supported in the sample by

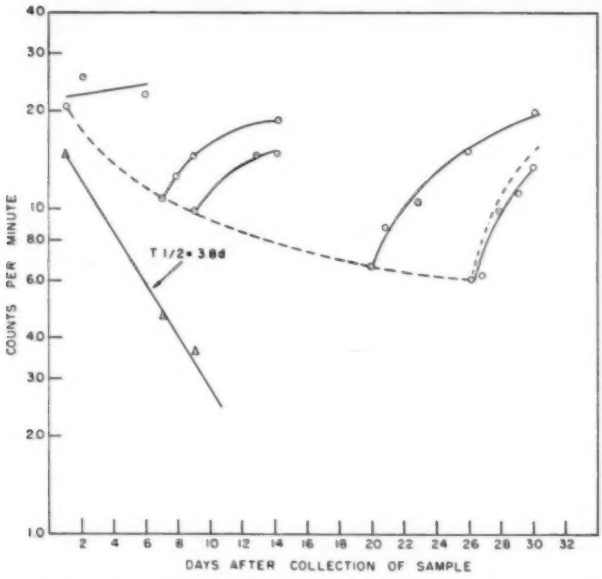

Fig. 1. Growth curves of Ra^{226} and ThX separated from portions of a sample of Joliet well water at different times after sampling.

——— Counting rates for a given portion. — — — First counting rate for a given portion. —△— Decay of ThX obtained by subtraction of counting rate of Ra^{226} from first counting rate for a given portion. —·—·— Calculated growth for Ra^{226}.

1.90—y RdTh. Supporting this interpretation, values of Ra^{226} and ThX (calculated using Equations 3 and 4) are given in Table I for the Joliet sample and for a deep well on the ANL site. The calculated values for Ra^{226} were constant, and the concentrations of ThX at the collection time (Table I, column 6) were constant within experimental error when the values at the time of analysis were corrected for decay with a 3.64-day half-life. Long counting times were used in the analysis of the ANL sample, in order to obtain better precision than that obtained for the Joliet sample.

Since the half-lives of ThX and 3.825—d Rn^{222} were almost the same, some thought was given to the possibility that the decay ascribed to the former might have been due, instead, to contamination of the $BaCl_2$ precipitate by radioactive decay products of radon present in excess of radium. This possibility was rejected for several reasons:

1) The concentration of radon in the Joliet sample was found to be 2.5×10^2 $\mu\mu$c per liter, and, since radon is quickly boiled off, the

Table I

Radium Content of Two Samples of Well Water Determined at Various Times After Collection of Samples

Sample	Date Collected	Days after Collection[1]	$\mu\mu$c per liter[2]		
			Ra^{226}	ThX[3]	ThX at Collection Time
ANL	5/3/52	0.26	5.23 ± 0.10	3.12 ± 0.12	3.28 ± 0.12
		0.26	5.24 ± 0.10	3.11 ± 0.12	3.27 ± 0.12
		2.20	5.07 ± 0.09	2.14 ± 0.07	3.26 ± 0.11
		5.22	5.31 ± 0.09	1.34 ± 0.07	3.61 ± 0.19
		5.22	5.39 ± 0.09	1.13 ± 0.07	3.04 ± 0.19
Joliet	20/12/50	1.1	5.0 ± 0.5	5.2 ± 0.6	6.4 ± 1.0
		7.1	5.3 ± 0.5	1.8 ± 0.2	6.8 ± 1.0
		9.2	4.2 ± 0.6	1.5 ± 1.3	
		20.0	5.6 ± 0.6	0.3 ± 0.8	
		26.2	5.2 ± 0.5	0.1 ± 0.5	

[1] Elapsed time from collection of sample to isolation of radium.

[2] The errors indicated are the statistical 0.9 error in counting or the average error of duplicate determinations, whichever was the larger.

[3] Concentration of ThX at time of isolation for a given portion.

activity of the daughters having an average half-life of about 30 minutes would have been reduced to less than 1 $\mu\mu$c by decay alone in 4 hours, the minimum time elapsed for evaporation and mounting of a sample;

2) similarly, the short-lived descendants of radon would have been reduced to negligible levels for the ANL sample because the third and fifth day analyses were made on water which had been evaporated from 5 liters to 500 ml on the day of sampling;

3) furthermore, the chemical operations used for the analysis are reported to separate Ra from Po (RaA) and Bi (RaC) (1), and the dissolving of $PbSO_4$ in concentrated HCl should have been an effective holdback step for Pb (RaB);

4) no combination of Ra^{226} and descendants of Rn^{222} seemed likely to result in the growth curves given in Fig. 1.

Direct analysis for thorium in the water from the ANL well showed that less than 0.02 $\mu\mu$c Th per liter was present. This confirmed the lack of RdTh indicated by the decay of ThX.

Since the presence of ThX was established, calculations for Ra^{226} and ThX were made for all samples. As seen in Table II, most of the results on water obtained near the ANL site fall into two groups: high

Table II

Radium Content of Drinking Water in the Chicago Area

Source	Collection Date	No. of Samples	$\mu\mu$c liter[1]	
			Ra^{226}	ThX
1. Deep Well #1A at ANL, 1,600 Feet	5/3/52	5	5.25 ± 0.05	3.3 ± 0.1
2. Tap Water at ANL (Shallow Wells)	5/5/52	2	0.04 ± 0.02	0.04 ± 0.02
3. Chicago — Lake Michigan Raw	1/6/51	2	< 0.1	—
4. Chicago — Tap	31/5/51	2	< 0.2	—
5. Joliet — Washington St. Well, 1,500′	6/3/51	2	5.2 ± 0.6	6.9 ± 1.3
6. Joliet — Washington St. Well, Raw	22/4/52	2	5.4 ± 0.1	6.6 ± 0.2
7. Joliet — Washington St. Well, Chlorinated Tap.	22/4/52	2	4.8 ± 0.2	4.5 ± 0.1
8. Joliet — Washington St. Well, Chlorinated Tap.	26/5/52	2	4.7 ± 0.2	3.6 ± 0.2
9. Lockport — Well #1, 1,550′	6/3/51	2	8.0 ± 0.3	7.3 ± 2.1
10. Lemont City Well, Raw, 1,665′	20/3/51	2	6.8 ± 0.3	5.8 ± 0.9
11. Aurora — Main Pumping Station, Raw Well, 2,200′	3/4/51	2	4.9 ± 0.5	5.2 ± 1.0
12. Aurora — Shallow Domestic Well, 100′	3/4/51	2	0.25 ± 0.1	0.4 ± 0.2
13. Elgin — City Well #1, 2,000′	4/4/51	2	0.8 ± 0.3	1.0 ± 0.4
14. Elgin — State Hospital Well, 2,000′	4/4/51	2	0.2 ± 0.1	1.0 ± 0.2
15. Elgin — State Hospital, Tap	1/6/51	1	0.3 ± 0.1	0.8 ± 0.2
16. Elgin — State Hospital Well, 2,000′	1/6/51	1	0.3 ± 0.1	1.0 ± 0.3
17. Elmhurst — Raw Well #3, 1,500′	31/3/52	1	4.5 ± 0.1	4.9 ± 0.2
18. Elmhurst — Raw Well #4, 1,550′	31/3/52	1	4.4 ± 0.1	6.3 ± 0.2
19. Elmhurst — Tap	31/3/52	1	4.3 ± 0.1	5.3 ± 0.2
20. Stateville — State Prison, Center Well, 1,500′[2]	6/4/51	2	1.8 ± 0.2	2.1 ± 0.2
21. Stateville — State Prison, Outside Well, 1,550′	6/4/51	2	4.2 ± 0.5	7.2 ± 1.2
22. Stateville — State Prison, Outside Well, 1,550′	10/9/52	2	4.0 ± 0.2	5.4 ± 0.4
23. Stateville — State Prison, North Well, 1,550′	10/9/52	2	3.4 ± 0.1	5.4 ± 0.2
24. Stateville — State Prison, South Well, 1,550′[3]	10/9/52	2	3.0 ± 0.1	1.6 ± 0.1
25. Stateville — State Prison, Tap	10/9/52	2	3.4 ± 0.4	3.5 ± 0.3

[1] The error indicated is the statistical 0.9 error in counting or the average error in replicate analyses, whichever was the larger for a given sample.

[2] Infrequently pumped.

[3] Pumping started for sample.

values for deep wells, which penetrate into the Galesville formation at 1,500 to 2,000 ft below ground level, and much lower values for surface water or shallow wells.

It should be noted that all of the water obtained from a deep well may not come from the greatest depth, because well casings are usually set only part way down the well, and water can enter from higher levels. This may explain the low values obtained for the deep well at the Elgin State Hospital from which samples were taken soon after pumping was started.

Using a radon emanation method on samples collected at the same time as our samples, J. B. Hursh (5) at the University of Rochester, found 6.54 ± 0.36 $\mu\mu$c Ra per liter for the untreated Joliet sample collected on 22/4/52 and 5.79 ± 0.13 $\mu\mu$c Ra per liter for the Joliet tap water

collected on 26/5/52. These values are somewhat higher than our values of 5.4 and 4.7, respectively.

The combined population of Aurora, Elmhurst, Joliet, Lemont, and Lockport is over 100,000, so these communities contain a large number of people who are drinking water of a radium content appreciably higher than that commonly encountered. It would be interesting to compare the retention of radium by these people with that of the people studied by HURSH and GATES (6). The maximum permissible level recommended for Ra^{226} in drinking water is 40 $\mu\mu$c per liter (11); this is only 5 to 10 times greater than the concentration of Ra^{226} in some of the deep wells listed in Table II.

Radium in Frankfurt and Pittsburgh Waters. Analyses were performed on water from two cities for which the radium concentration in the tap water had been reported to be high. KREBS reported 300 to 500 $\mu\mu$c Ra per liter for tap water at Frankfurt am Main, Germany, in 1939 (8). However, we found less than 0.3 $\mu\mu$c Ra per liter for the 12 sources of Frankfurt's drinking water now available and for the Main River (Table III). One Frankfurt well was no longer in operation at the time our samples were obtained. Check analyses on the Goldstein and Praunheim II samples using a radon emanation method showed 0.2 ± 1 $\mu\mu$c Ra per liter for each. In the other case, BOTSET reported 143 $\mu\mu$c Ra per liter in a sample of tap water at Pittsburgh, Pennsylvania (2). Many analyses of Pittsburgh water taken directly from reservoirs and rivers using 5 liter samples were made by J. SCHUBERT and R. LESKO, of the Argonne National Laboratory, but the largest concentration of Ra they found was 0.12 $\mu\mu$c per liter (13).

Table III

Ra^{226} in Water from Frankfurt am Main, Germany

Source	$\mu\mu$c Ra/liter[1]	$\mu\mu$c Ra/liter[2]
Main River	—	0.2
Hatterscheim	0.2	—
Hatterscheim II	—	0.2
Moenschhof	0.1	0.2
Hinkelstein	—	0.1
Schwanheim	0.2	0.2
Goldstein	0.1	0.2
Oberforsthaus	—	0.3
Praunheim II	0.2	0.2
Praunheim III	—	0.2
Griesheim (not working)	—	—
Vogelsberg	0.1	—
Spessart	—	0.1
Wirtheim	—	0.2
Inheiden	0.1	0.1

[1] Samples collected 14/12/50. — [2] Samples collected 20/7/51.

The cause of the above discrepancies is not known. In each case, the earlier results were mentioned as blank runs in reporting on work not concerned with the concentration of radium in drinking water. Possibly, the samples were contaminated at the water supply by an industrial establishment or during the analyses. KREBS reported his values on the basis of direct evaporation of water and counting of the residue, and BOTSET isolated Ra by precipitating $BaSO_4$, metathesizing with carbonate, dissolving the $BaCO_3$ with HCl, and sealing the solution in an Erlenmeyer flask for a few days for radon to grow in for gamma-ray measurement. Thus, the activity measured by the former procedure could have been caused by many radioactive nuclides, and ThX would have been included in Botset's procedure. However, direct evaporation and counting of a sample of Pittsburgh tap water (collected 2/1/52) in this laboratory showed less than 1 $\mu\mu$c of total alpha activity per liter one day after sampling, and approximately 1 $\mu\mu$c of alpha activity per liter was found by direct evaporation of the Inheiden sample from Frankfurt two months after collection.

Acknowledgement

Credit is due to the members of the Background Analytical Group of the Radiological Physics Division and especially Mr. EDWARD WOOD for collecting and analyzing many of the samples.

We are greatly indebted to Dr. CHARLES H. BENNING, Advisor, Office of the United States High Commissioner for Germany, and Major JESSE D. HUMPHRIES, 60th Medical Group, U. S. A. F., for aid in obtaining the water samples from Frankfurt, and to Dr. EDWARD CREUTZ, of the Carnegie Institute of Technology, for obtaining samples from Pittsburgh. Our thanks to Dr. JACK SCHUBERT and Dr. J. B. HURSH for permission to use results obtained at their respective laboratories.

SUMMARY

Water from wells which penetrate into the Galesville sandstone of Cambrian age at a depth of approximately 1,500 feet near Chicago, Illinois was found to contain from 3 to 8 $\mu\mu$c Ra^{226} per liter and similar concentrations of Ra^{224}. This is believed to be the highest authenticated concentration of radium found to date for any drinking water in the United States. The combined population of the communities using these wells is over 100,000.

Drinking water from Frankfurt am Main, Germany was found to contain less than 0.3 $\mu\mu$c Ra^{226} per liter as compared to more than 300 $\mu\mu$c per liter previously reported. Less than one $\mu\mu$c of total alpha activity per liter was found in water from Pittsburgh, Pennsylvania, although 143 $\mu\mu$c Ra^{226} per liter had been reported.

ZUSAMMENFASSUNG

Das Wasser von Brunnen, die in den kambrischen Sandstein in Galesville in der Nähe von Chicago, Illinois, bis zu einer Tiefe von ungefähr 1,500 Fuss dringen, enthielt zwischen 3 und 8 $\mu\mu$c Ra^{226} pro Liter und ähnliche Mengen des Ra^{224}. Man nimmt an, dass dieses die

höchste authentische Radiumkonzentration ist, die bisher in Trinkwasser in den Vereinigten Staaten festgestellt worden ist. Die gesamte Bevölkerungsmenge, welche diese Brunnen benutzt, beläuft sich auf über 100,000.

Trinkwasser von Frankfurt am Main, Deutschland, enthielt weniger als 0.3 $\mu\mu$c Ra^{226} pro Liter und nicht, wie kürzlich berichtet, mehr als 300 $\mu\mu$c pro Liter. Weniger als 1 $\mu\mu$c totaler α-Aktivität pro Liter wurde in Wasser von Pittsburgh, Pennsylvania, gefunden, obwohl ein Gehalt von 143 $\mu\mu$c Ra^{226} pro Liter berichtet worden ist.

RÉSUMÉ

L'eau de puits qui pénètrent dans le grès de Galesville, près de Chicago, de l'âge Cambrien à une profondeur approximative de 1,500 pieds s'est révélée contenir de 3 à 8 $\mu\mu$c de Ra^{226} par litre et une concentration semblable en Ra^{224}. C'est, croit-on, la plus haute concentration vérifiée en radium, trouvée à ce jour dans une eau potable aux Etats-Unis. L'ensemble de la population des collectivités utilisant ces puits dépasse 100,000 personnes.

L'eau potable de Francfort-sur-le-Mein, Allemagne, contient moins de 0.3 $\mu\mu$c de Ra^{226} par litre au lieu de plus de 300 $\mu\mu$c par litre signalés précédemment. L'auteur a trouvé une activité alpha totale de moins d'un $\mu\mu$c par litre dans l'eau de Pittsburg, Pennsylvanie, bien qu'on ait signalé 143 $\mu\mu$c de Ra^{226} par litre.

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THE LYMPH DRAINAGE FROM THE BREAST TO THE AXILLARY AND PARASTERNAL LYMPH NODES, STUDIED WITH THE AID OF COLLOIDAL Au^{198}

by

K. A. Hultborn, L.-G. Larsson and *I. Ragnhult*

In carcinoma of the breast without evidence of distant metastases, it seems logical to direct surgical and radiologic treatment against the whole breast and its local lymphatics including the lymph vessels and the regional lymph nodes. As regards the lymph nodes, interest was previously concentrated mainly on the axillary, infraclavicular and supraclavicular groups. In recent years, however, several clinical investigations have dealt with the importance of parasternal lymph node metastases and their treatment.

Anatomy. According to STILES (1892) some of the lymph from the mammary gland is transported by lymphatics which accompany the blood vessels which pierce the pectoralis major muscle and the intercostal spaces and then run with the internal mammary vessels. GEROTA (1896 and 1897) demonstrated lymphatic pathways running from the breast via intercostal spaces to parasternal lymph vessels, and he made clear that local recurrences in the pectoralis major muscle might be attributable to this. OELSNER (1901) found that these lymph vessels pierce the first to the fourth intercostal spaces near to the sternum, whereas STIBBE (1918) stated that the parasternal lymph nodes are usually situated in the first, second, third and sixth intercostal spaces. YOON (1924) wrote: "In order to be quite sure, it is necessary in this area to excise the anterior

Submitted for publication, 27 September 1954.

intercostal lymph node and the second, third and fourth intercostal muscles, which are pierced by the lymph vessels. In this way metastases may be avoided and the prospects of definite healing improved."

CUNNINGHAM's Textbook of Anatomy (1952) contains the following reference to these lymph vessels: "From the medial part of the mammary gland a few vessels pierce the pectoralis major and pass through the anterior ends of the intercostal spaces to reach the internal mammary chain of lymph glands. The cutaneous vessels must be remembered as an important part of the lymph drainage of the mamma . . . and it should be noted that some of them pass deeply between the lobules of the gland. These cutaneous vessels pass to the axillary, infraclavicular and internal mammary lymph-glands and a few ascend from the skin of the upper part of the mamma to the lower deep cervical glands."

Clinical observations. In 1922, SAMPSON HANDLEY (cited by DAHL-IVERSEN) tried to remove parasternal lymph nodes in five cases for microscopic examination, and found such nodes only in one case. GORDON-TAYLOR (1947) reported that more than a dozen times he had removed the chain of anterior lymph glands along with the internal mammary vessels. R. S. HANDLEY and THACKRAY (1949) made a preventive removal of the parasternal lymph nodes in 50 cases. By 1954, their series had increased to 135 cases. Under their operative procedure the classical operation for mammary cancer had been followed by dissection of the lymph nodes around the internal mammary artery in the second and third intercostal spaces. Their observations are summarized in Table 1 (cited by ROSENQVIST).

Table 1

	Localization of the primary breast carcinoma		
	Medial	Lateral	Total
Total number of cases	51	84	135
No metastases	12	33	45
Axillary metastases alone	9	37	46
Parasternal metastases alone	4	1	5
Axillary and parasternal metastases	26	13	39

MARGOTTINI and BUCALOSI (1949) reported their experience of removal of the parasternal lymph nodes with all surrounding fatty tissue from the first three intercostal spaces in 110 cases of carcinoma of the breast. The removal took place after resection of the second to the fourth costal cartilages. Of the 43 cases without axillary metastases, two (5 per cent) showed parasternal metastases. Worthy of note is that both these cases had lateral tumours. In 67 cases with axillary metastases, parasternal metastases were found in 23, or 34 per cent. Of 28 cases of medial tumours, nine (32 per cent) had parasternal metastases, and of 39 cases with lateral

tumours, fourteen (36 per cent) showed parasternal metastases. (Cited by BERVEN.)

MÖRL (1951 and 1952) presented his observations in 18 cases of mammary carcinoma, of which five were referable to STEINTHAL (*i. e.*, clinical) stage I, and 13 to STEINTHAL (*i. e.*, clinical) stage II. In the first group there were no axillary metastases, but one parasternal metastasis, the tumour here being localized to the upper lateral quadrant. In the second group, there were eleven cases with axillary metastases and six with parasternal metastases. In four cases, the tumour was localized to the upper lateral quadrant and in two cases to the medial quadrant. With a view to elucidating the significance of the situation in spread to the parasternal nodes, MÖRL injected Indian ink bilaterally in the breasts of 24 women who were expected to die shortly of incurable disease. His results are summarized in Table 2.

Table 2

Quadrant	Number of breasts	Axillary and infraclavicular	Parasternal
Lower medial	8	7+	5+
Upper medial	10	10+	7+
Upper lateral	4	3+	3+
Lower lateral	12	10+	9+
	34	30+	24+

MÖRL's conclusions were as follows: It was immaterial in which quadrant of the breast the injection was made. Contrary to what had been claimed, it was precisely from the lateral quadrants that the dye most often entered the sternal lymph nodes.

DAHL-IVERSEN et coll. (1951, 1952 and 1954) reported their experience of parasternal metastases. In the last 100 of their cases, the technique had been radical: after cutting through the second, third and fourth costal cartilages 1 to 1.5 cm from the sternal border, they had excised the vessels with accompanying lymphatics and glands and all fatty tissue from beneath the first cartilage down to the level of the fifth cartilage. Their observations are summarized in Table 3.

Table 3

Site of metastases	Site of primary growth	
	Medial	Lateral
Axillary only	4	21
Parasternal only	4	0
Axillary and parasternal	7	6
Axillary and supraclavicular	0	3
No metastases	22	33
Total	37	63

URBAN and BAKER (1952) described a radical method for removal of parasternal lymph-node metastases: the first and fifth intercostal spaces were opened and the internal mammary blood vessels ligated. The lateral portion of the sternum together with the second to the fifth costal cartilages with the pleura were excised, leaving a defect of about 12 by 8 cm in the thoracic wall.

At the Department of Surgery of Karolinska Sjukhuset (ROSENQVIST 1954) URBAN's operative method has been used in recent years for selected cases, mostly in tumours of medial situation. In the hope of throwing further light on the significance of the situation of the primary tumour of the breast for the spread to various lymph-node regions, we decided to conduct a functional anatomic study of the lymph drainage with the aid of a radioactive colloid. After the interstitial injection of a colloid with suitable particle size, some of the particles are taken up by phagocytes, transported by the lymph vessels to their regional lymph nodes and retained in their reticulo-endothelium. The production of artificially radioactive colloids afforded a convenient method of studying the distribution of the colloid as well as certain therapeutic potentialities. One of the substances most used has been radioactive gold (Au^{198}) as red colloid, and its behaviour after interstitial injections has been rather extensively studied (GOLDIE et coll., SHERMAN et coll., KOTTMEIER et coll., MELLGREN et coll.).

Technique and Material

We employed in this investigation radioactive gold, Au^{198}, as red colloid obtained from Harwell. We injected a tracer dose of 1 to 5 mC in a small volume of fluid varying from a few tenths of a milliliter to a few milliliters. We sought to inject the colloid in as small volume as possible of the breast, usually as far as possible from the primary tumour. In 40 cases, radical excision of the breast was performed after 1 to 10 days. In 14 of these patients, the operation was combined with parasternal en bloc resection *ad modum* Urban, and in two patients, with supraclavicular dissection. (Most patients also received preoperative roentgen treatment consisting of a small dose, usually 3 × 350 r; distance 50 cm, filter 0.5 mm Cu, 170 kV, to each of two tangential fields including the breast and the axilla. The treatment was completed 1 to 10 days before the operation.)

After the operation, when the Au^{198} depot was removed, we carried out *in vivo* measurements with a directional scintillation counter (cylindrical collimator, length 10 cm, aperture diameter 1.2 cm, lead thickness 2.5 cm). In several cases, we demonstrated high counting rates in small circumscribed parasternal areas well corresponding to the site of the parasternal lymph nodes (Fig. 1). We were unable, on the other hand, to

Fig. 1. Uptake of colloidal Au^{198} in parasternal lymph nodes detected by *in vivo* measurements with a directional scintillation counter. Counting rates of 1 000 to 1 300 cpm over the marked areas, 250 to 300 cpm over the other parts of the sternal and parasternal regions. (Measurements after radical excision of the left breast).

demonstrate any localized uptake in the contralateral parasternal region, the contralateral axilla or supraclavicular fossa. In most cases, slightly increased counting rates were found over the liver, probably due to the fact that a small part of the injected isotope escaped to the general circulation and was taken up by the liver.

The operative specimens were investigated in the following way. The γ-irradiation from the breast, the axillary tissue and the parasternal specimen was measured with a wide-angle scintillation counter and compared with a standard solution of Au^{198} taken from the same solution as the injected isotope. These measurements included, of course, a major error due to geometry and absorption but gave rough information about the distribution of the radiogold. In all cases, it was found that most of the colloid (usually more than 85 per cent) remained at the site of the injection and only a relatively small part was deposited in the lymph-node regions. The lymph-node regions were then carefully dissected in order to find as many lymph nodes as possible. The uptake in the individual lymph nodes was measured with a γ-sensitive scintillation counter; with the arrangement used, the errors due to geometry and absorption could be ignored for these small specimens. The lymph nodes were then prepared for histologic sectioning and radioautographs, which were made according to a simple contact method using non-screen roentgen film. As small parasternal lymph nodes were sometimes difficult to find on dissection, the remaining intercostal soft tissue was prepared for serial sectioning.

Axillary lymph nodes. These lymph nodes were studied in 40 operative specimens, where the injections had been given in varying parts of the breast including the central and subareolar parts, the four quadrants as well as the most medial part of the breast. In all cases, regardless of the site of the injection, some of the lymph nodes showed an uptake of radiogold. In most cases, some of the normal lymph nodes did not show any detectable uptake (Figs. 4, 5 and 7), and in some lymph nodes, only a small part of the node had taken up the radioisotope (Fig. 2). This

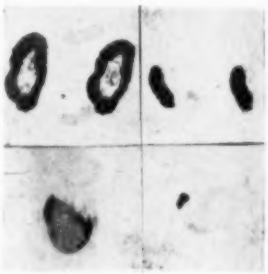


Fig. 2. Large normal lymph node from the axilla with uptake only in one segment (stained section left, radioautograph right).

Fig. 3. Axillary lymph-node metastasis with uptake in a small remnant of lymphatic tissue (stained section left, radioautograph right).

probably indicates a segmental arrangement of the lymph drainage from the breast to the axilla and in one case, where an extensive part of the breast was infiltrated with radiogold, uptake was found in all the axillary lymph nodes. Cancerous parts of the lymph nodes did not, of course, take up the radiocolloid, but often small remnants of lymphatic tissue in lymph nodes extensively destroyed by cancer still showed an uptake (Fig. 3).

Parasternal lymph nodes. These nodes were studied in 14 operative specimens, where the injections had been given in the lower medial quadrant in two cases, centrally in the mammary tissue in five, and in the upper lateral quadrant in seven, including four cases injected extremely laterally in the mammary tissue. In each of the 14 cases, we were able to demonstrate uptake in some of the parasternal lymph nodes (Figs. 4 and 5). In some cases, the parasternal lymph nodes were rather large (Fig. 6) and easily found on dissection. At times, however, small parasternal nodes were very difficult to find, especially when they diverged from their normal situation along the course of the internal mammary vessels. In one case (Fig. 7), they could be found, on dissection, only with the guidance of a radiation detector; they were situated at a greater distance than normal from the internal mammary vessels and a few millimeters inside the intercostal muscles. In another case, one of the lymph nodes was not detected until serial sections had been made of the intercostal soft tissues.

Supraclavicular lymph nodes. The study of these lymph nodes is only preliminary and includes, so far, only two cases. In one of these cases uptake was found, demonstrating the direct lymph drainage from the breast to these lymph nodes.

The investigations conducted hitherto suggest, therefore, that lymph drainage occurs from practically all parts of the breast to both the axillary and parasternal nodes. Hence metastases in those nodes may be possible regardless of the situation of the primary tumour in the breast.

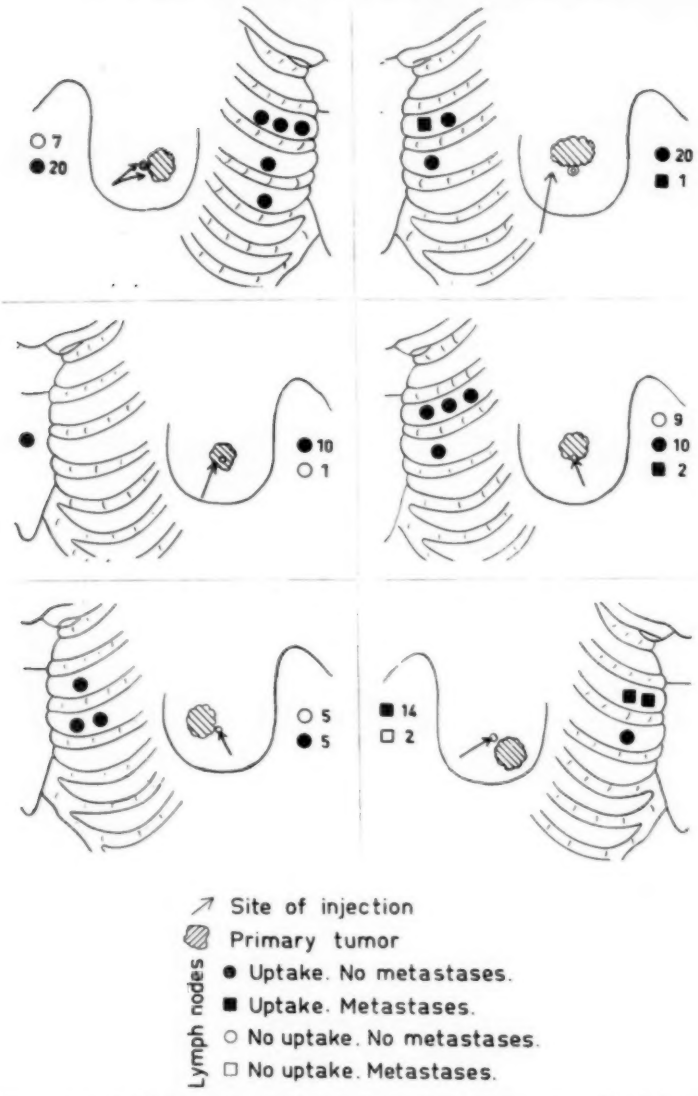


Fig. 4. Cases 1 to 6. Uptake of colloidal Au^{198} in the lymph nodes after injection in the mammary gland, studied after radical excision of the breast combined with parasternal en bloc resection *ad modum* Urban. (The number of parasternal lymph nodes in the different intercostal spaces is marked by individual signs, and the number of axillary nodes by figures after the signs. In Case 3 the exact intercostal space for the parasternal lymph node detected was not determined.)

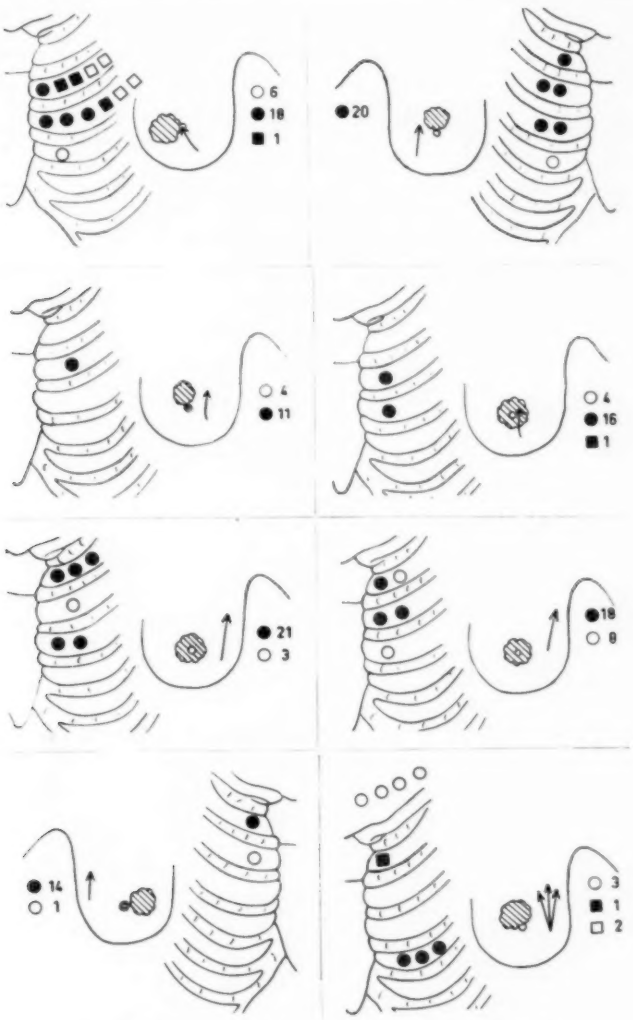
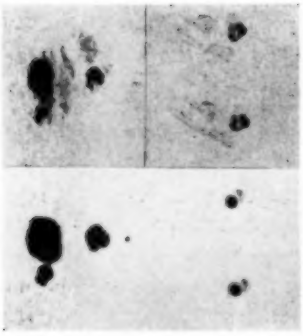


Fig. 5. Cases 7 to 14. For description see Fig. 4.

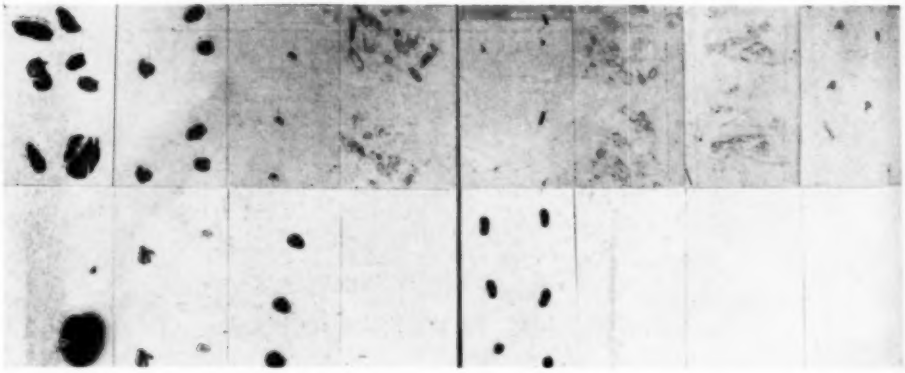
In the 14 cases in which both the axillary and the parasternal lymph nodes were removed, the total uptake in those nodes amounted to 0.1 to 11 per cent of the colloid injected. In 13 of the cases, the axillary lymph nodes contributed 97 to 99 per cent of that uptake and the parasternal nodes only 1 to 3 per cent. The maximal total uptake noted in the axillary



$P_{II\ III}$ $P_{III\ IV}$

Fig. 6. Uptake in parasternal lymph nodes from the second and third intercostal spaces (stained section above, radioautographs below. Some of the lymph nodes seem enlarged in this and some of the following radioautographs, due to overexposure.)

lymph nodes was 10.5 per cent, as compared with only 0.4 per cent in the parasternal lymph nodes. In case 14, in which the added uptake in the axillary and parasternal lymph nodes was only 0.1 per cent, the distribution was inverse and the axillary nodes contained only about one-tenth of the activity in the parasternal nodes. In this case, however, three axillary lymph nodes were almost completely destroyed by cancer and the remaining axillary nodes showed pronounced fibrous transformation. In our material, there was no constant relation between the site of the injection and the distribution of the isotope in the two lymph-node regions studied. The material was, of course, rather unsuitable for quantitative studies, as some lymph vessels were blocked by the primary tumours and several cases had lymph nodes more or less involved by cancer. The great difference found in most cases between the uptake in the axillary and that in the parasternal lymph nodes is, however, certainly of great significance and indicates that only a very small proportion of the lymph is transported from the breast by



A $P_{II\ III}$ $P_{III\ IV}$ $P_{IV\ V}$ $P_{V\ VI}$

Fig. 7. Sections from the axilla (A) and the parasternal region (P). Lymph nodes found only on slides 1, 2, 3 and 5. The small parasternal lymph nodes could be found, on dissection, only with the guidance of a radiation detector. (Stained section above, radioautographs below.)

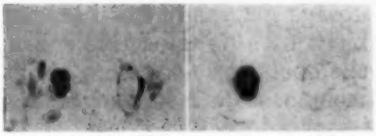


Fig. 8. Parasternal lymph nodes. The left node, which contains a small metastasis, shows a good uptake of radiogold. (Stained section left, radioautograph right.)

the parasternal compared with the axillary route. This may explain the lower incidence of parasternal than of axillary metastases demonstrated in reported surgical series.

The best method of treating the parasternal lymph nodes in carcinoma of the breast is still unclear and will certainly remain so for many years until sufficient experience has been gained of new therapeutic methods. The two principal alternatives seem to be surgery or external radiation treatment. Due to the anatomic variations, safe radical removal of these nodes requires en bloc resections of URBAN's type. This operation is not an innocuous procedure and in many cases it seems questionable whether it is justified 'prophylactically'. With external irradiation, it is difficult to give an adequate tumour dose to the parasternal lymph nodes without too severe damage to surrounding tissues, especially the lungs and the heart. The rapid technical development of radiotherapy seems, however, to afford good possibilities of treating these lymph nodes adequately. The electron beam of 10 to 15 MeV would, for instance, give an almost ideal dosage distribution due to the rapid fall of the depth dose when the

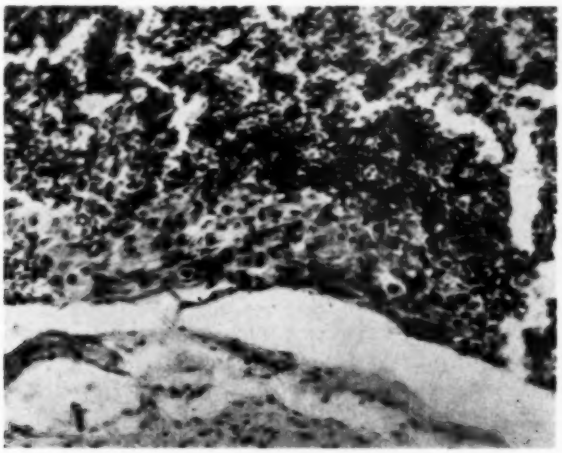


Fig. 9. Detail of the left lymph node in Fig. 8, showing a minute metastasis in the sinus. (× 60.)

dosage maximum has been reached. A third possibility would be treatment with a radioactive colloid injected into the mammary gland before the operation and taken up by the lymph nodes. Such a method would include several limiting factors, such as irregular distribution of the isotope, inability of the wholly cancerous parts of the nodes to take up the colloid, etc. It seems not altogether improbable, however, that a radiocolloid with faster uptake in the lymph nodes than radiogold, a suitable half-life and a more energetic β-irradiation might be a useful adjunct in the treatment of early parasternal metastases (Figs. 8 and 9).

SUMMARY

The literature on the lymph drainage from the mammary gland, especially to the parasternal lymph nodes, is reviewed. A functional anatomic study of the lymph drainage from different parts of the mammary gland was conducted with colloidal radiogold, Au^{198}, in cases of carcinoma of the breast. After injection of the radiocolloid in the breast, high counting rates were demonstrated *in vivo* with a directional scintillation counter in small circumscribed areas well corresponding to parasternal lymph nodes. The uptake in the lymph nodes was also studied in operation specimens by direct measurements and radioautographs.

In 40 cases the distribution of the radiogold in the axillary lymph nodes was studied in operation specimens. In 14 cases treated *ad modum* Urban with en bloc resection of the parasternal region, the uptake of radiogold in these nodes was also investigated. Regardless of the site of injection the radiocolloid was transported both to the axillary and to the parasternal lymph nodes.

ZUSAMMENFASSUNG

Die Literatur über die Lymphdrainage der Brustdrüse, besonders zu den parasternalen Lymphknoten, wird durchgegangen. Eine funktionelle anatomische Studie der Lymphdrainage von verschiedenen Teilen der Brustdrüse wurde mit radioaktivem Gold, Au^{198}, in Fällen mit Brustkrebs ausgeführt. Nach Injektion des radioaktiven Kolloides in die Brust wurden mit einem gerichteten Szintillationszähler hohe Messausschläge in kleinen umschriebenen Zonen *in vivo* nachgewiesen, welche gut mit den parasternalen Lymphdrüsen übereinstimmen. Die Aufnahme in den Lymphdrüsen wurde auch an Operationspräparaten durch Direktmessungen und Autoradiographien studiert. In 40 Fällen wurde die Verteilung des radioaktiven Goldes in den Lymphdrüsen der Schulterhöhle an Operationspräparaten studiert. In 14 *ad modum* Urban mit En bloc-resektion der parasternalen Region behandelten Fällen wurde die Aufnahme des radioaktiven Goldes in diesen Drüsen ebenfalls untersucht. Unabhängig von der Injektionsstelle wurde das Radiokolloid sowohl zu den axillären als auch zu den parasternalen Lymphdrüsen transportiert.

RÉSUMÉ

Les auteurs passent en revue la littérature sur le drainage lymphatique de la glande mammaire, en particulier vers les ganglions lymphatiques parasternaux. Ils ont fait une étude anatomique fonctionnelle du drainage lymphatique de différentes parties de la glande mammaire dans des cas de cancer du sein, au moyen de l'or colloïdal radio-

actif Au^{198}. Après injection du colloïde radioactif dans le sein, de forts taux de comptage furent mis en évidence *in vivo* avec un compteur à scintillation directionnel dans de petites aires circonscrites correspondant bien à des ganglions lymphatiques parasternaux. La fixation dans les ganglions lymphatiques a été aussi étudiée sur des pièces opératoires par des mesures directes et des autoradiographies. La répartition de l'or radioactif dans les ganglions lymphatiques axillaires a été étudiée dans 40 cas sur des pièces opératoires. Dans 14 cas traités suivant la technique de Urban avec résection en bloc de la région parasternale, la fixation de l'or radioactif dans ces ganglions a aussi été examinée. Quel que fût le lieu d'injection, le radiocolloïde parvint aussi bien aux ganglions lymphatiques axillaires qu'aux ganglions parasternaux.

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EQUIPMENT AND TECHNIQUE IN PRECISION ROTATION ROENTGEN THERAPY

by

S. Benner, O. Dahl, S. Hultberg, R. Thoræus and *K. J. Vikterlöf*

It was in the late nineteen-thirties that physical, mathematical and clinical trials were carried out on rotation therapy notably, inter alios, by DESSAUER, LION and MUTHEREM (1), NAKAIDZUMI and MIYAKAWA (7, 8), and DU MESNIL DE ROCHEMONT (5, 6). These were prompted by physical considerations suggesting that clinical advantages might be expected in treatment by substituting conventional multiple field therapy by this method. The experience acquired during the next few years, particularly at a number of European clinics, showed that the expectations had not been unwarranted. It was found that at equivalent tumour dosages the patients tolerated rotation therapy better than treatment by the multiple field technique, and that better palliative results were obtained. Moreover, improved *curative* results were reported, mainly by GYNNING (3) from the Jubilee Clinic at Lund, where EDLING (2) in 1942 installed a rotation therapy unit with which HULTBERG was working during the first year.

Following a proposal put forward by HULTBERG, an experimental equipment for rotation therapy was installed at Radiumhemmet during 1950. From March to October 1951 this equipment was temporarily in clinical use and valuable experience was gained. In May 1951, DAHL visited clinics at Erlangen, Copenhagen, and Lund in order to study rotation therapy. We are greatly indebted to our colleagues at these clinics, whose experience was valuable in the preparatory work which followed. The present equipment for rotation therapy at Radiumhemmet

This investigation has been supported by grants from the Cancer Society, Stockholm, the Swedish Cancer Society and the Brothers P. A. Ljungberg Foundation; submitted for publication, 18 May 1954.

was taken into clinical use in March 1953. (The plant was produced by Elema-Järnh AB., Stockholm, to our due instructions and design based upon the physical and medical factors involved.) The developmental work was most ably supported by the late Professor H. AHLBOM.

A number of authors, including NAKAIDZUMI and MIYAKAWA (7) and H. NIELSEN (12), have already shown by measurements in homogeneous cylindrical phantoms that no essential improvement in the ratio of depth dose to surface dose is to be gained by using radiation qualities of higher HVL than 0.6 mm Cu. These measurements were chiefly concerned with the depth dose at the rotation axis, and were carried out with radiation qualities of up to a HVL of 1.8 mm Cu at a tube voltage of 180 kV.

The present roentgen therapy equipment of Radiumhemmet includes, in addition to a number of units having a maximum tube voltage of 200 kV, one plant designed for a potential of up to 400 kV. We were therefore able to extend our measurements — which also included investigation of the isodose curves in a phantom — up to a tube voltage of 400 kV, corresponding to a HVL of 3.4 mm Cu. Complete series of measurements, to be reported in a subsequent paper, were made at radiation qualities with HVL of 0.4, 0.8, 1.6, 1.8 and 3.4 mm Cu respectively. The measurements were made by SIEVERT (13) condenser chambers. Because of the extended quality range used, the chambers were selected for wavelength independence within ± 7 per cent throughout the range. A cylindrical paraffin wax phantom with a diameter of 30 cm was employed in the measurements. In the HVL range of 0.4 to 1.3 mm Cu, the measurements, in so far as they concerned the ratio of depth dose to surface dose, were, in addition, carried out with phantoms of 12 and 20 cm diameter. Our results, too, show that no essential improvement of the ratio between the depth dose at the rotation axis and the surface dose is to be gained with radiation qualities of higher HVL than 0.7 mm Cu. The same result was also found in the isodose distribution. Recent investigations by THOMS, MADSEN and H. NIELSEN (14) in the corresponding quality range lend further support to these results in so far as the thoracic region is concerned. If rotation therapy is to be used for tumours in the pelvic region, there is reason to assume that with due regard to the size of the surrounding bones, a somewhat better ratio of depth dose to surface dose might be obtained with radiation qualities of higher HVL than 0.7 mm Cu — an assumption supported by the results published by THOMS, MADSEN and H. NIELSEN (14).

The rotation therapy equipment now in use at Radiumhemmet is primarily designed for treatment of intra-thoracic tumours. In our experience it is *essential to use continuous fluoroscopic control in rotation therapy*. In order to secure at a reasonable cost a radiation-proof area for the observer and as a result of our investigations and experiments, we

decided to use roentgen apparatus giving a maximum tube voltage of 200 kV constant potential. The machine is operated at the full 200 kV and the maximum permissible tube current of 20 mA in order to reduce the daily treatment time for each patient as much as possible. For the same reason, we use an additional filter of only 0.2 mm Cu plus 1 mm Al, which gives a radiation quality corresponding to HVL of 0.7 mm Cu. Since a further increase in the filtration, in accordance with the foregoing considerations, will not alter the depth dose distribution, the addition of a compensating filter — the use and clinical value of which will be discussed below — requires no other correction than that corresponding to the reduction of the dose rate. Our measurements show that this is valid regardless of the diameter of the region of the body treated.

As regards the focus—axis distance in rotation therapy, an investigation by HOEFFER JENSEN, J. NIELSEN and THAYSSEN (4) shows that its increase above 70 cm does not result in any appreciable improvement in the ratio of the depth dose to surface dose. H. NIELSEN, in a later paper (12), subscribes to this opinion. Since any increase in this distance will cause an undesired increase in the daily treatment time, our investigations were concentrated on the range between 50 and 70 cm. Nor in that range were we able, within the accuracy of the measurements, to demonstrate any positive change. But since the tube in question has a comparatively large focus giving fields with somewhat indistinct edges, it is important, with a constant distance between the field diaphragm and the rotation axis, not to choose too short a focus—axis distance. We have therefore chosen a distance range of 55 to 65 cm. In order to reduce the penumbra further, the tube container is provided with an applicator of variable length, by which the diaphragm can always be positioned as near the rotation axis as the size of the patient's body permits.

A brief description of the rotation therapy laboratory of Radiumhemmet now follows. Fig. 1 shows a plan of the installation. From it and from Figs. 2 and 3 it will be seen that the tube with its wall stand (1, 16) as well as the special devices fitted to the tube container, together with the rotation chair (17) and the fluoroscopic screen unit (6) with its suspension devices (10), are all placed in the treatment room. The window of the room is provided with a black-out curtain, and the intensity of the lighting can be controlled from the observer's position (54). The inner walls, the floor and the ceiling of the treatment room are lined with protective material equivalent to at least 4 mm of lead; but the lead glass window (13), situated behind the screen unit and receiving the direct roentgen beam, is equivalent to 6 mm of lead.

Behind the lead glass window in the darkened control room is the observer's position (54) from which continuous fluoroscopic control during each treatment is carried out, and from which the pre-treatment

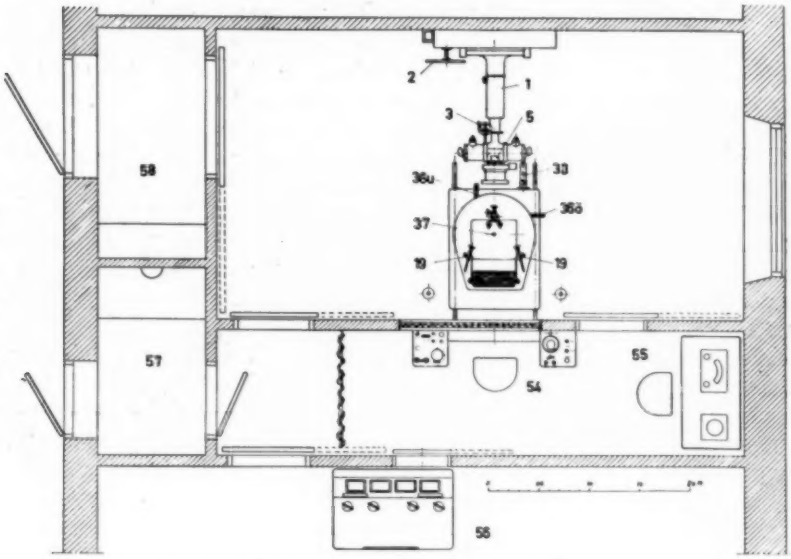

Fig. 1. Plan of the rotation therapy laboratory.

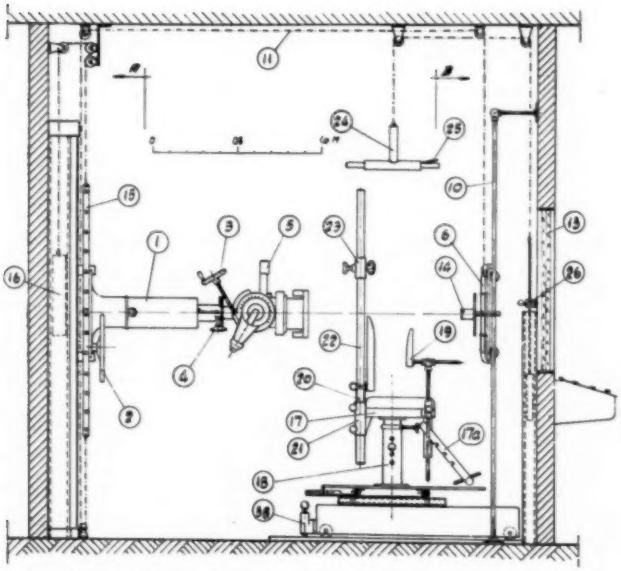

Fig. 2. Schematic side-view of the treatment room.

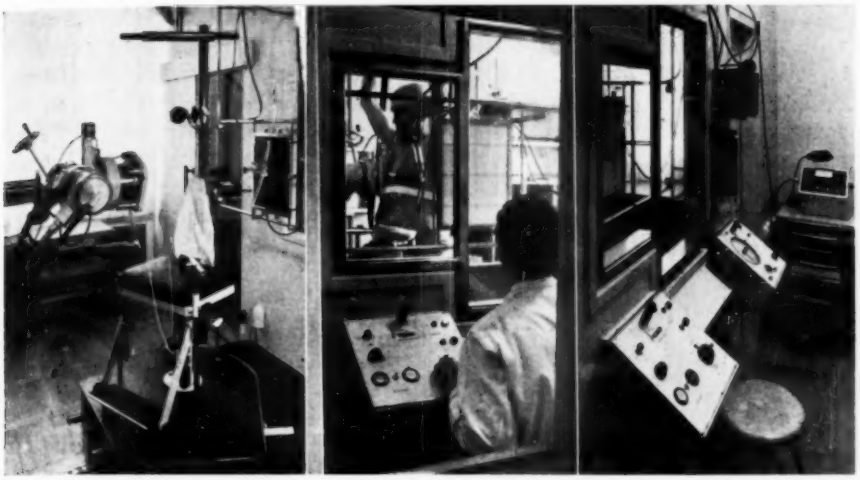

Fig. 3. Fig. 4. Fig. 5.

Fig. 3. Side-view of the treatment room.

Fig. 4. Treatment of a patient with a carcinoma in the cardiac region. Photograph taken through the sound opening from which the curtain has been removed.

Fig. 5. View of the control room with the observer's place in front and the physicist's place behind.

adjustments, as well as corrections required during the treatment, may be operated by remote control (Fig. 4). All of these remote controls are assembled in two small desks, one on each side of the observer's seat. There is also a space in the control room for the physicist (55) with his instruments for dose measurements during the course of treatment. Fig. 5 shows a view of the control room. Detailed radiation protection measurements of this room have been carried out. They show that the total irradiation at an effective treatment time of two hours per day is, at the maximum, 20 milliroentgens per week.

The switchboard (56) of the roentgen ray apparatus is situated outside the control room, and communication between the operating radiographer and the observer is effected via a lightproof sound opening. The installation also includes a dressing cubicle (58) for the patients, and a small darkroom (57) for loading cassettes. A reversible loudspeaker system provides continuous communication between the patient and the observer.

The radiographer at the switchboard controls the tube voltage, which at a constant filtration defines the radiation quality, and the dose rate, which can be kept constant by means of a monitoring ionization chamber

placed in the beam exit opening of the tube container and connected to a reading instrument on the switchboard. The monitoring chamber is so designed that it serves also as the additional filter. If the anatomic orientation during the treatment should prove difficult, the need for temperatory beam direction control with a substantially increased field size may arise. In such an event, and when the irradiation and rotation have been interrupted, fluoroscopic control may be effected at the requisite tube voltage and tube current, the smallest possible dose thus being administered to the patient. In connection with such control as well as during pre-treatment adjustments, the monitoring filter can, if necessary, be pulled out of the beam by means of a motor (5) remotely operated from one of the control desks. The unit is fitted with an automatic device so arranged that when the filter is pulled out, the tube voltage cannot be raised above 110 kV at a tube current of 10 mA.

The tube container is fitted to a Siemens wall-stand (1, 16). It can be raised and lowered either from the observer's position or by hand (2) from the stand itself. By means of a mechanical transmitting device (11) the screen unit is connected to the tube container in such a way that it accompanies the latter in its vertical movements. The roentgen tube is fitted in a standard Siemens oil-insulated tube container with a lead shutter, remotely controlled both from the observer's position and the switchboard. Under the operating conditions given a dose rate of approximately 40 r per minute, measured in air, is obtained at a focal distance of 55 cm. In the treatment of intra-thoracic tumours with a focus—axis distance of 55 cm, geometric field sizes of about 4 $\times$ 15 cm at the rotation axis and a compensating filter, a tumour dose of 200 r is usually obtained in 6 to 9 minutes, corresponding to 2 to 3 revolutions. The tube and its container together have an inherent filtration equivalent to about 2 mm Al. The tube container is provided with a specially designed applicator consisting of two end-pieces and two intermediate pieces, which can be so combined as to give an applicator length adapted to the circumstances. Since the outer end-piece supports the field diaphragm, the variable applicator length thus enables the diaphragm to be brought as close to the rotation axis as the size of the patient's body permits. The applicator is designed to prevent the primary beam from striking its lateral walls. The diaphragm permits of arbitrary adjustment of rectangular axis fields up to a geometric size of 22 $\times$ 22 cm, and up to $\pm$ 45 degrees tilting of the field about the central axis of the beam — all remotely operated from one of the control desks. Treatment fields other than those rectangular in shape may, when required, be obtained by fitting invariable additional diaphragms. The applicator contains a 'visor' consisting of a lamp and a mirror, by means of which both the shape and the central line of the beam can be indicated. The mirror consists

of polished aluminium and absorbs the softer scatter from the oil in the tube container, this being of importance if screening is carried out with the monitoring filter pulled out. There is also a holder in the applicator for individually adapted compensating filters by which the dosage distribution in the tumour area can be flattened in each case.

The design of the screening unit (6) and its distance to the focus and to the rotation axis conform in principle to those described by GYNNING (3). The size of the geometric axis field is adjusted by setting the indicators of the screening unit to twice the geometric axis field size required; after this the beam is so adjusted by the remote-controlled field diaphragm that the field seen on the screen corresponds to the field defined by the indicators. Our investigations have demonstrated this method for adjusting the size of the geometric axis field to be sufficiently accurate. In addition to the abovementioned remote-controlled vertical adjustment, the tube may also be rotated (3) about its long axis, so that the beam forms an angle of up to $\pm$ 30 degrees with the horizontal plane. The screen unit then also accompanies the tube in its vertical movement, and by means of a simple coupling (15) can be so adjusted that the central line of the beam always strikes the centre of the screen; the method for adjusting the size of the geometric axis field can thus be maintained. After testing a number of different screens for brightness and contrast at the relevant radiation qualities, we chose a Patterson screen, Type B2 No. 550, which in clinical use has been found to afford satisfactory fluoroscopic control.

The mounting of the rotation chair contains the mechanism for revolving the base plate, operated by remote control from one of the control desks, where the rotation is continuously shown on a specially designed indicator. The rate of rotation intended for treatment amounts to one revolution in three minutes; but in addition a second rate of one revolution in 36 seconds provides for rapid adjustments. The seat-platform is mounted on the base plate on two pairs of rails running crosswise. The movement on these rails is effected by motors remotely operated from one of the control desks at the observer's position. The motors are so connected that the movement of the seat-platform relative to the base plate will always be approximately at a right angle to the beam, independent of the momentary rotation angle of the base plate. In eight special positions of the base plate at 45 degree intervals, the movement of the seat-platform will be *exactly* perpendicular to the beam. The movement device described is of great importance in performing the pre-treatment adjustment. The requisite movements of the seat-platform, relative to the base plate and perpendicular to the roentgen beam, are carried out by remote control under fluoroscopic guidance. This is done in such a manner that two mutually perpendicular base

plate positions are selected, in which the movement of the platform will be exactly at a right angle to the beam, and which permit satisfactory screening of the patient. Even an eccentrically situated tumour will in this way very quickly and easily be brought into the rotation axis. There are two scales (36 u and ö) on the base plate, enabling the adjustment of the seat-platform to be checked and, if required, duplicated. The seat itself (17) may be raised and lowered (18) on the platform and is fitted with an adjustable foot support (17 a) and the requisite devices for fixation of the patient. These latter consist of A) a back support (22) made of low absorbent material and to which are fixed a) a backrest of perspex, b) a headrest with a forehead band (23), and c) a further special headrest for use in the treatment of intracranial tumours; B) two lateral supports of perspex (19) fitted directly to the seat; and lastly C) two fixation belts at chest and knee levels respectively. When the scales for the adjustment of the platform are set at zero, the position of the rotation axis in relation to the seat is definitely fixed, and the beam may then be centered by means of an indicator fitted to the seat in the rotation axis (37). The roentgen tube can be moved along the central line of the beam. To enable the rotation axis, at the different focus—axis distances used, always to be brought midway between the focus and the fluoroscopic screen, the mounting of the rotation chair runs along two rails in the floor, so that the whole chair can be moved along the beam and fixed in the desired position (38). A trapeze (24) suspended from the ceiling, serves as an arm rest in the treatment of the thoracic region. A safety switch, also suspended from the ceiling, is gripped by the patient during the treatment. If the grip is relaxed, a contact is closed and an alarm bell in the control room rings.

At a number of clinics abroad where rotation therapy is used, the patient is positioned on the chair without any particular fixation (WACHSMANN and BARTH, 15). The patient is thus able to move within wide limits, causing considerable deviation of the tumour centre from the rotation axis. Any movement at right angle to the beam can easily be compensated for under fluoroscopic control, as for example, in the manner mentioned above, but any deviation along the beam cannot be seen on the screen and cannot, therefore, be corrected. According to our measurements covering the range from 0 to $\pm$ 8 cm, cyclic and equal deviations of the tumour centre to either side of the rotation axis, with the tumour centre remaining in the central line of the beam, do not influence the tumour dose significantly. In practice, however, the deviations are mainly irregular, and their effect on the tumour dose will, therefore, not in general be negligible. In view of this it is necessary to reduce these irregular deviations as much as possible by *a perfect fixation of the patient on the rotation chair*. Clinical tests have shown that with good fixation the

deviations of the tumour centre to either side of the rotation axis along the beam do not exceed ± 1 cm, giving errors in the tumour dose rate not exceeding ± 4 per cent.

The guiding principle in all radiotherapy is to give the whole of the tumour volume — determined as accurately as possible by available clinical methods with an additional safety margin — a radiation dose determinable by measurements and empirically optimal for the disease in question at the fractionation chosen; at the same time, adjacent tissue must receive the smallest possible dose. In comparison with conventional treatment carried out with multiple fields, moving field therapy, and particularly that employing rotation tec..nique, affords greater possibilities of satisfying these requirements. In what follows we give a brief description of our attempts to utilize these possibilities to the full.

In view of the unreliability that always attends the calculation of tumour doses (especially in parts of the body markedly inhomogeneous as regards absorption), we consider *direct measurements* to be the only satisfactory method of determining the tumour dose. Such measurements, however, can only be made in cases in which the tumour is situated sufficiently close to a body cavity in which dosemeters may be inserted.

We have carried out dose-measurements in the hypopharynx, oesophagus, and stomach as well as in the trachea, main bronchi and their major branches, using an adequate number of SIEVERT (13) condenser chambers (length 20 mm, diameter 5 mm), positioned in a plastic sound tube in the manner previously described by NICOLAEFF and THORÆUS (11). In all such measurements in body cavities an appropriate number of indicators, made of effective radiation absorbent material such as tungsten, are fitted between the chambers in the sound tube. By means of these indicators, the position of the tube in the irradiated region can be both primarily adjusted and checked during the treatment under fluoroscopy. Further checking of the position of the sound tube and of the beam in relation to the patient is performed at the beginning and end of the tumour dose measurement by means of radiography. We found it to be of importance, prior to the insertion of the sound tube in the hypopharynx and oesophagus, to remove all traces of the barium contrast medium used for the pre-treatment adjustment by making the patient swallow water repeatedly while under fluoroscopic control. This prevents the recording of dose values too low as a result of radiation absorption by the contrast medium. In patients with tumours in the cardiac region and the superior parts of the stomach, we found it essential to maintain satisfactory evacuation of the bowel. If this is not done, progressive accumulation of contrast medium in the flexures of the colon, especially the left, the transverse colon or all these regions, may cause increased radiation absorption, substantially decreasing the radiation dose in the inferior part of the axis field.

The first measurement is performed as early as possible in each series of treatments. When made in a body cavity within the tumour region, the result of the measurement shows the dose distribution along the axis of the cylindrical volume which has received continuous direct irradiation. Our measurements reveal that this dose distribution as a rule is not even (the difference between maximum and minimum may amount to 50 per cent of the maximum value, the geometric indistinctness at the upper and lower edges of the beam not being taken into account). This is mainly due to differences in the average radiation absorption between different levels of the region of the body irradiated, and in a less degree to the fact that with usual geometric field widths (4 to 5 cm), geometric field lengths of about 15 cm are usually required, which in turn causes a decrease of the dose from the centre toward the ends of the field.

The length of the tumour is determined in each case as accurately as possible by the clinical methods available, a safety margin of at least 4 cm both cranially and caudally, being added. The dose should be the same along the geometric axis field length thus determined. *Individually adapted compensating filters* of copper are used in order to flatten as far as possible irregularities in the dose distribution which occur in most cases and are found by means of the measuring method described. The decrease caused by the geometric indistinctness at the upper and lower edges of the beam may be neglected by reason of the long safety margins chosen.

As regards the irradiation of the tumour, the ideal condition would, of course, be to vary the compensation during rotation. At the same time the tube output would be varied so that the dose rate in the volume receiving continuous direct irradiation would be uniform and constant during the rotation. Since, however, for technical and medical reasons, this can scarcely be accomplished, and since in rotation therapy the total angle utilized for irradiation during each revolution (360° or a part thereof) constitutes the most suitable unit, we have elected for the time being to carry out the tumour dose measurements on the basis of, and to refer the compensation to, that unit. Provided that depth dose measurements can be made throughout the field length, a compensating filter for each individual case is designed on the basis of the first such measurement, the flattening effect of the filter thus being referred to a complete revolution. A control measurement is made to check in what degree the desired effect has been attained. Experience has shown that the first compensating filter does not always result in a satisfactory flattening but that, in most cases, modifications of the compensation based on one or two control measurements will be found to give the desired result.

When the dose distribution has been brought under control and the

dosage for the case in question, with due regard to clinical considerations, has been decided upon, the patient need not necessarily be subjected to further direct dose measurements during the remainder of the treatment series, provided the irradiation conditions are kept sufficiently constant. A further tumour dose measurement is made for additional control usually between the twentieth and twenty-fifth day of treatment if the patient's general condition permits.

For constant conditions of treatment, the following requirements must be fulfilled:

1. Constant distance between focus and tumour centre. As mentioned, this is obtained in a sufficient degree by good fixation of the patient.

2. Constant field size, which pre-supposes both that requirement 1 has been satisfied and the field diaphragm is not changed in shape or size during the treatment but tilted, if required, around the centre line of the beam.

3. Constant primary dose rate, obtained by using the monitoring chamber as described.

To check the constancy of all the conditions of treatment, a comparison is made of the integrated transit doses, measured during each treatment at the same point behind the patient by a specially designed ionization chamber (14). Such investigations have shown that with our equipment and technique, the conditions of treatment can be kept constant within an average error of $\pm$ 5 per cent.

The *transit dose measurements* are made according to a method developed by NEUMANN and WACHSMANN (9), and have proved to be of considerable value; the use of the method has been extended. According to these authors the transit dose is measured only at the centre of the beam. The measuring device designed by us also permits measurements at different levels in the field. The measuring chamber (14) is positioned about 7 cm in front of the fluoroscopic screen by means of a support which can be so operated from the observer's position that the chamber accompanies the tilting movement of the field. The ionization chamber is connected to a Philips dosemeter placed in the control room (Fig. 5) and enabling either the integrated dose or the instantaneous dose rate to be read. Help can be obtained in the designing of a compensating filter, by employing this measuring device for two or three treatments. This is of special importance in cases in which direct tumour dose measurements cannot be made to the extent required. As mentioned earlier, the device also enables the constancy of the treatment conditions to be checked; for this purpose the transit dose is measured at the centre of the field during at least one revolution of the daily treatment. In those cases in which variations from day to day — for example, in the content of gas and

barium in the stomach and superior parts of the colon — may be expected to cause considerable variations in the absorption in the corresponding part of the body region irradiated, an additional measurement of the transit dose is made behind that part during at least one revolution of the daily treatment. In this way the dose distribution may be kept under continuous control and, if necessary, flattened.

On the other hand, it is our experience to date that the transit dose behind patients with intra-thoracic tumours cannot be used unconditionally for determination of the tumour dose in the manner reported by NEUMANN and WACHSMANN (9), even with tumours situated centrally in the body. This opinion is based on tumour dose measurements and coincident transit dose measurements, referred to a complete revolution, and made in every case in which such measurements were possible. A systematic study of the doses in intra-thoracic tumours, calculated from the transit doses, and the tumour doses found by direct measurements has shown that the former, as a rule, are essentially higher. Further investigations in this field are proceeding.

We carry out skin dose measurements at suitable sites around the periphery in most cases, coincidently with the above-mentioned measurements, in order to obtain further information as to the dose distribution.

In the choice of the geometric field width at the rotation axis, the following points must be considered. The maximum transverse extension of the tumour is determined as accurately as possible with the aid of the clinical methods available. In oesophageal tumours, for example, any curvature of the oesophagus in the region treated has to be taken into account. A safety margin of at least half a centimeter on each side should be added since determination of the width of a tumour is always somewhat uncertain. The transverse extension thus obtained determines the width of the cylindrical rotation volume in the body, within which the irradiation should be distributed as evenly as possible with the best possible protection of the surrounding tissues.

Reports by NEUMANN and WACHSMANN (10), and H. NIELSEN (12), among others and confirmed by our own measurements in homogeneous cylindrical phantoms, seem to indicate that in irradiation of approximately central intra-thoracic tumours, a transverse dose distribution sufficiently even for clinical purposes within a cylindrical volume d cm in diameter will be obtained if a geometric field width of d cm at the rotation axis is used, provided that d is more than 3 cm. We feel justified, therefore, for the time being in using this method of determining the geometric field width at the rotation axis, required in each individual case. We are aware, however, that the dose distribution is not quite even, caused among other reasons by the geometric indistinctness. We have begun

extensive measurements of the dose distribution in physically correct anatomic phantoms. If these measurements show this to be necessary, we shall flatten the transverse dose distribution by employing a special compensating filter. Pending the results of these investigations, and to limit as far as possible the integral dose received by the patient, we have up to now avoided field widths at the rotation axis greater than those obtained with the above-mentioned procedure. The practical consequence is that the geometric field widths at the rotation axis have mostly measured from 4 to 5 cm.

In order to obtain a detailed survey of the irradiation during one revolution, instantaneous radiation measurements in the tumour would be required during the course of rotation. It seems likely that a Bomke dosemeter specially adapted to our requirements will permit such measurements to be carried out; its ionization chamber can be readily inserted into practically all the body cavities. Investigations in this field will be carried out.

With the rotation therapy equipment described, we have, since March 1953, treated nine patients with carcinoma at the junction of the hypopharynx and oesophagus, 43 with oesophageal carcinoma, two with carcinoma in the cardiac region, two with tracheal lymphadenosis, five with bronchial carcinoma, one with acromegaly, two with thyrotropic exophthalmus, and two with Cushing's syndrome. The five last patients have received irradiation of the pituitary gland.

In tumours situated at the junction of the hypopharynx and oesophagus, the great variation in the transverse diameter of the body within the region of tumour growth makes it difficult to give adequate roentgen treatment without risk of local over- or under-dosage. The best way to avoid such complications would be to use compensating filters and complete dose control by direct measurements. With the multiple field technique, however, this involves certain practical clinical difficulties. Only with rotation therapy combined with a compensating filter, used as described, did we obtain a technique to which no objections could be raised from the practical clinical standpoint. The irradiation is interrupted as the beam passes the shoulder regions. Since the tumours in question are usually situated nearer to the anterior surface of the neck, we have chosen to interrupt the irradiation once in the course of three consecutive revolutions — namely, when the beam passes the anterior irradiation angle — in order to reduce the dose received by the skin of the anterior surface of the neck. The compensating filter used was designed to give the required flattening effect during such a treatment of three revolutions. For a more detailed study of this kind of therapy technique, measurements on physically correct anatomic phantoms are planned. In the irradiation of tumours in the neck and upper part of the

thorax we have found it possible, by simultaneous measurements in the oesophagus, the trachea and the bronchi, further to investigate the dose distribution in each individual case. The insertion of the sound tubes has been performed by HJ. KOCH (Assistant Professor in the Ear, Nose and Throat Department, Karolinska Sjukhuset).

Rotation technique with this equipment has also proved to be suitable for directing treatment intracranially, for which purpose a special method has been developed. Since it is only in exceptional cases that contrast indicators can be applied intracranially we place lead rings at suitable sites on the skin under fluoroscopic control for indirect indication of the region to be treated. The dose received by this region is determined from comparative measurements in each patient and in a physically correct anatomic cranial phantom, as near as possible to the relevant size. In the phantom the intra-cranial dose distribution and the transit dose are determined, and behind the patient the transit dose is measured; conclusions are drawn as to the intra-cranial dose distribution in the patient. For this purpose a series of three cranial phantoms of different sizes have so far been prepared. This will be extended to cover the variations in the cranial dimensions in the Swedish population if our investigations show this to be required for adequate determination of the dosage. In irradiation of the pituitary gland and using geometric axis fields about 3 cm in diameter, it has proved possible to deliver up to 4,000 r in about four weeks to the gland without any greater skin reaction than transient epilation.

It has been maintained by some clinics that the multiple field technique may afford greater possibilities for accuracy than the rotation method in the positioning of the beam in relation to the tumour and surrounding tissues. In our experience, however, rotation treatment with the equipment and technique described gives at least the same accuracy as any multiple field technique. Rotation therapy also involves a simplification, as well as an improvement, as regards both the practical realisation of the treatment and the attainment of requisite and precise dose measurements in accessible cavities. It has been found, moreover, that our measuring technique does not cause the patients any distress. We therefore feel justified in employing the method in all cases in which the site, shape, and size of the tumour indicate its suitability.

The available data concerning the optimal and the tolerance doses from various clinics using rotation therapy show appreciable differences for the same tumour sites. It seems likely to us that these discrepancies are due, in part at least, to the difficulty of determining the tumour dose accurately by calculation and indirect measurement. They may also be occasioned by varying accuracy in the treatment methods, especially as regards the control of constancy and continuous supervision during treat-

ment. Our equipment and technique satisfy very exacting requirements as regards the accuracy of adjustment and the continuous control of irradiation, dosage and dose distribution. In our opinion, every detail of the treatment must satisfy similar exacting demands if the advantages presented by rotation therapy are to be utilized to the full. A fully satisfactory application of this technique can hence only be carried out at major radiation therapy centres having access to extensive clinical experience, experts qualified in medical radiophysics, adequate resources of other personnel and the requisite equipment. At such centres the clinical material will also be large enough to ensure full use of a rotation therapy room. This is an advantage as partial use of the room for conventional types of irradiation would inevitably jeopardize the accuracy required in rotation therapy.

In view of the relatively short period that our laboratory has been in use, the therapeutic results cannot be clinically surveyed as yet. However, it has already proved possible, in the great majority of cases, to carry out the treatment planned, even though this has had a curative purpose and not, as at many other clinics, merely a palliative one. Moreover, both the effect on the general condition of the patients and the skin reactions obtained have been considerably milder than in corresponding treatments in which the conventional multiple field technique has been employed.

Our measurements and the more important details of the equipment and technique will be given in further publications and in due course present and planned investigations of dose-estimations, dose-distributions and treatment reactions and results will be reported.

SUMMARY

The equipment and a technique for precision rotation roentgen therapy, developed at Radiumhemmet primarily for the treatment of intra-thoracic tumours, is described. The accuracy attained is at least the same as may be attained by any multiple field technique, particularly as regards the positioning of the beam in relation to the tumour. Moreover, the rotation technique described, in all cases in which it is clinically indicated, involves a simplification as well as an improvement in the practical realisation of both the treatment and the requisite and accurate dose measurements. The results of dose measurements made are discussed, and first clinical experiences briefly outlined.

ZUSAMMENFASSUNG

Die Ausrüstung und eine Technik für präzise Röntgenrotationsbestrahlung, in erster Linie für die Behandlung intrathorakaler Tumoren, wird beschrieben. Die hierbei erreichte Genauigkeit ist zu mindest die gleiche, die mit jeder Kreutzfeuerbestrahlung erreicht werden kann; dies gilt besonders für die Lage des Strahlenbündels im Verhältnis zum Tumor. Darüber hinaus führt die beschriebene Rotationstechnik in allen Fällen, wo sie klinisch angezeigt ist, sowohl eine Vereinfachung als auch eine Ver-

besserung der praktischen Ausführung der Behandlung und der notwendigen Dosismessungen mit sich. Die Ergebnisse ausgeführter Dosismessungen werden besprochen und die ersten klinischen Erfahrungen kurz zusammengefasst.

RÉSUMÉ

Les auteurs décrivent l'appareillage et la technique de roentgenthérapie rotatoire de précision mis au point à Radiumhemmet, primitivement pour le traitement des tumeurs intra-thoraciques. La précision atteinte est au moins égale à celle qu'on peut atteindre de toute technique à champs multiples, en particulier en ce qui concerne la position des rayons par rapport à la tumeur. De plus, la technique rotatoire, dans tous les cas où elle est cliniquement indiquée, amène une simplification et une amélioration de la réalisation pratique du traitement et des mesures de dose. Les auteurs examinent les résultats des dosimétries qui ont été effectuées et donnent un aperçu des premiers essais cliniques.

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CONTINUOUS REGISTRATION OF THYROID UPTAKE AFTER INTRAVENOUS INJECTION OF RADIOACTIVE IODINE

A rapid test of iodine concentrating function of the thyroid

by

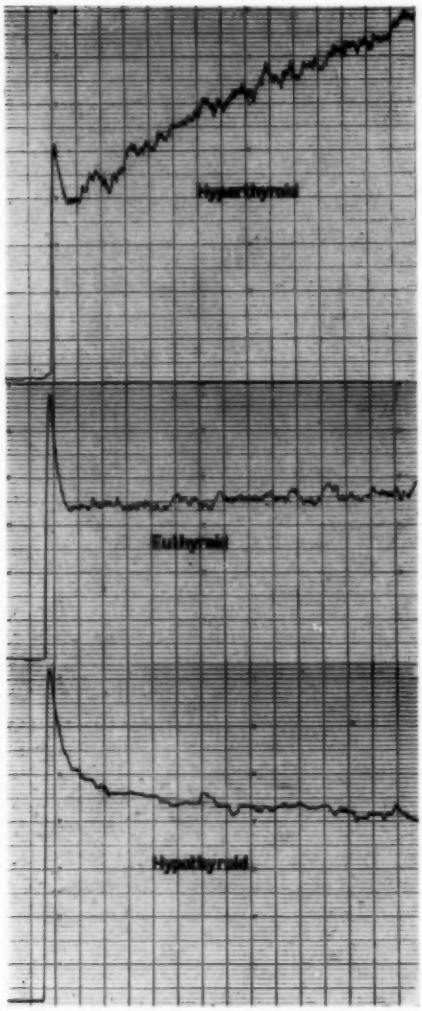
Lars-Gunnar Larsson and *Lars Jonsson*

The ability of the thyroid gland to concentrate radioactive iodine has been widely studied in functional thyroid disorders, and many practical tests have been worked out. The uptake of radioiodine in the thyroid may be measured *in vivo* at different times after the administration and the urinary excretion or the disappearance rate of radioiodine in the blood may serve as an indirect measure of the iodine-concentrating capacity of the thyroid (1—24 and others).

One of the tests most used is the estimation of the uptake in the thyroid after 24 hours. Earlier uptake measurements give, however, for several reasons a better differentiation between the functional states, and many investigators prefer uptake measurements after, for instance, 30 minutes to 4 hours (1, 2, 7, 12, 17). To avoid the resorption phase in the gastro-intestinal tract, it is preferable to perform these early uptake measurements after the intravenous injection of I^{131}; the uptake after one hour or more may, however, be used also after oral administration provided that the tracer dose is given on an empty stomach (2).

The following report demonstrates that measurements over the neck only 5 to 10 minutes after an intravenous injection of I^{131} give good information about the iodine concentrating function of the gland provided that a continuous registration of the counting rates from the time of the injection is performed. Such continuous registration has previously

Submitted for publication, 16 July 1954.



Diagrams 1—3. Initial neck curves after intravenous injection of equal tracer doses (0.1 mC) of I^{131} in one hyperthyroid, one euthyroid and one hypothyroid patient. The interval between the vertical lines is one minute.

been described (4, 13). No attempts were made, however, to use the curve during the first few minutes as an index of thyroid function. For this purpose it is necessary to have access to a measuring instrument which gives high counting rates with small tracer doses and for this purpose the gamma-sensitive scintillation counter is an ideal instrument. We used a lead-shielded NaJ (Tl) crystal provided with a wide-angle lead collimator. The counting-rates were registered by a counting-rate meter combined with a writing instrument ('Speedomax'). For the counting-rate meter, a time constant of 2.5 to 10 seconds was used. The scintillation counter was adjusted to a distance of 27 cm from the anterior surface of the neck before the injection of the tracer dose (0.05 to 0.1 mC I^{131}). Following the measurement on the patient, a standard solution of I^{131} with the same activity as the tracer dose was measured, and, after background correction, the counting rates measured over the neck were expressed as a percentage of the counting rate given by the standard solution; for the sake of convenience this is referred to in the following as the 'neck uptake' (H).

Result

Immediately after the injection, a high peak was obtained due to the I^{131} passing through the great vessels in, and in the neighbourhood of, the neck. In Diagrams 1 to 3 this peak is clearly visible but con-

siderably suppressed due to the relatively long time-constant used (10 seconds). After 30 to 60 seconds a fairly smoothly ascending curve was obtained in the hyperthyroid and euthyroid subjects and the increase was usually much more rapid in the former than in the latter (Diagrams 2 to 6). In the hypothyroid patients a slightly descending curve was usually obtained during the first minutes after the initial peak (Diagrams 3, 5, 6). An equalizing curve was drawn on the curve registered and, neglecting the first minute, which included the mixing phase of I^{131} in the blood, the curve was extrapolated to zero time. The neck uptake at zero time (H_0) probably represented the theoretical 'neck background' at this time, assuming that the I^{131} injected could be equally distributed momentarily in the blood. H_0 must then be independent of the radioiodine-concentrating capacity of the thyroid, which also was demonstrated in one euthyroid patient examined before and after treatment with chemical iodine (Diagram 4).

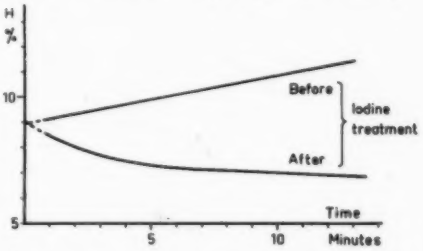


Diagram 4. Initial neck curves in an euthyroid patient before and after treatment with chemical iodine.

In Diagram 5 the neck uptake (H) in the first 19 cases examined is plotted against the time. A more clear-cut picture was, however, obtained if the differences between the 'neck uptake' and the 'neck background' at zero time ($H—H_0$) were plotted against the time, as illustrated in Diagram 6. Diagram 7 shows the result compared with the 24 hours thyroid uptake and 24 hours urinary excretion. As an expression for the initial neck curve we here employed the difference between the 10 minutes 'neck uptake' and the one minute 'neck uptake' ($H_{10}—H_1$). H_1 was used instead of H_0 in order to avoid the extrapolated part of the curve, which may include a somewhat subjective factor. In this material the initial neck curve gave a very good differentiation between the functional states of the thyroid.

Discussion

After the injection of I^{131} the counts measured over the neck are derived from the following sources:

1. Inorganic I^{131} circulating in the blood.
2. Inorganic I^{131} in the tissues, especially the extracellular fluid, due to its diffusion from the blood.
3. I^{131} taken up by the thyroid.

The counts derived from the first two sources constitute the 'neck

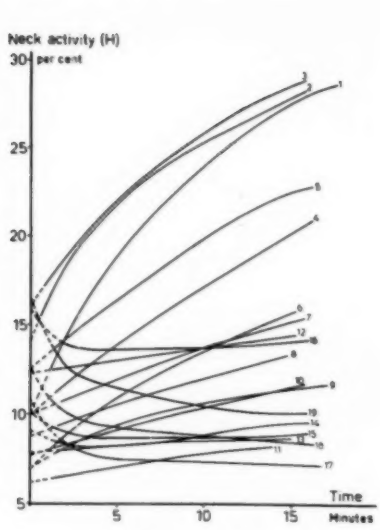


Diagram 5.

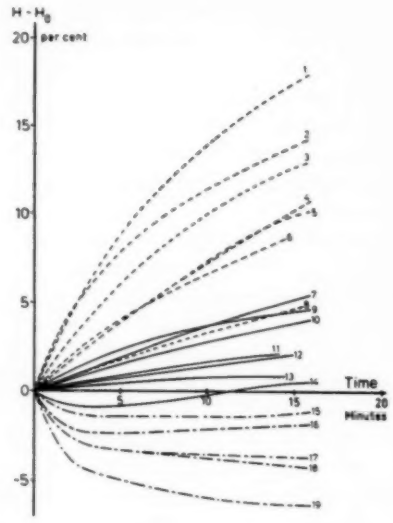


Diagram 6.

Diagram 5. Initial neck curves in 19 patients with hyper-, eu- and hypothyroidism. - - - - - hyperthyroid. ——— euthyroid. —·—·—·—· hypothyroid.

Diagram 6. Same curves as in Diagram 5 with subtraction of the theoretical 'neck background at zero time'.

background'. After an intravenous injection the concentration of I^{131} in the blood diminishes very rapidly, and if the 'neck background' were to change quite as quickly the initial neck curve would probably be useless for a study of the thyroid function. The initial rapid disappearance rate of I^{131} from the blood is, however, mainly due to its diffusion into the body fluids and therefore the 'neck background' diminishes much slower than the blood concentrations of I^{131}. This is probably the reason, why the thyroid uptake of I^{131} may characterize the neck curve as early as the first few minutes after an injection. If the accumulation rate of I^{131} in the thyroid is very low as in hypothyroid or iodine-treated subjects, the initial neck curve will be slowly descending, due to the fact that the decrease in the 'neck background' preponderates over the thyroid uptake. In patients with a normal or increased radio-iodine concentrating capacity of the thyroid this condition is in the inverse, which results in more or less ascending initial neck curves.

The test has the following theoretical and practical advantages.

1. As early as 5 to 10 minutes following the injection good informa-

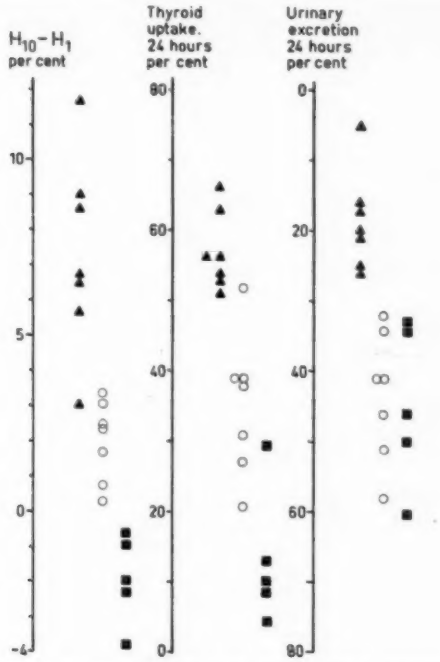


Diagram 7. Differentiation obtained by the initial neck curves, 24 hours thyroid uptake and 24 hours urinary excretion. Same cases as in Figs. 5 and 6. ▲ hyperthyroid. ○ euthyroid. ■ hypothyroid.

tion is obtained concerning the iodine-concentrating capacity of the thyroid; this may be especially valuable in the case of out-patients.

2. The test probably gives a better quantitative picture of the iodine-concentrating capacity of the thyroid than later uptake measurements. The uptake of I^{131} in the thyroid after a certain time depends upon the iodine-concentrating capacity of the gland, the average concentration of radioiodide in blood plasma up to that time for the measurement and the turnover of organic I^{131} from the thyroid to the blood. The sooner the uptake measurement is performed the less the influence on the result, which may be expected by variations in the two last-mentioned factors. The relative differences between the average plasma concentrations of radioiodide in different individuals, or in one individual during various states, are usually less pronounced from 0 to 10 minutes than for instance from 0 to 3 hours or from 0 to 24 hours. Beside the iodine-concentrating capacity of the thyroid, several extrathyroidal factors influence the plasma concentrations of I^{131}. Renal function is an essential

factor and, in cases with renal insufficiency, the thyroid uptake of I^{131} may increase due to the increased plasma concentrations of I^{131}. This factor influences the initial neck curve much less than later uptake measurements.

This was well illustrated by one of our hypothyroid patients, who also had renal insufficiency. The 24 hours thyroid uptake was 30 per cent and the 24 hours urinary excretion 34 per cent, *i. e.* values simulating normal thyroid function. The thyroid clearance was, however, only 6 ml/minute (normal values 20 to 60 ml/minute) and the renal clearance of I^{131} only 12 ml/minute (normal values 25 to 50 ml/minute). The initial neck curve had the typical 'hypothyroid' type.

It seems possible that the initial neck curve gives about as good quantitative information about the iodine-concentrating capacity of the thyroid as the more complicated tracer tests represented by 'thyroid clearance' estimation (3, 10, 18) or analysis of the cumulative urinary excretion curve (9, 19, 20, 21).

In certain hyperthyroid patients as well as in some euthyroid patients previously subjected to partial thyroidectomy (surgical or radiologic) the turnover rate of organic I^{131} from the thyroid to the blood is very rapid. This factor may seriously influence the 24 hours uptake but has practically no influence on the initial neck curve.

During treatment with antithyroid drugs of the thiouracil type (1), in rare spontaneous cases of hypothyroidism (8, 23), and sometimes after radioiodine treatment (11), the thyroid may still possess a good iodine-concentrating capacity but impaired ability to bind the iodine organically. In these cases the turnover of inorganic I^{131} from the thyroid to the blood essentially influences the uptake curve (1) and the initial neck curve affords the possibility for a study of the initial accumulation rate of I^{131} in the thyroid, which may be of considerable physiologic interest. A preliminary investigation has been performed and well illustrates the possibilities of the method.

3. When repeated tracer tests are desired for physiologic investigations the correction for any activity from I^{131} remaining in the thyroid from a previous tracer dose will be a minor problem. During as short a time as 5 to 15 minutes, the changes in the activity remaining may usually be neglected.

The test possesses of course some disadvantages, which may be summarized as follows:

1. The whole tracer dose must be injected intravenously. In patients with veins difficult to find and in small children the test can hardly be used.

2. If the iodine-concentrating capacity of the thyroid is very low, the test can neither demonstrate whether or not any thyroid uptake is

occurring, nor differentiate between various degrees of iodine-concentrating function.

3. Abnormal diffusion of I^{131} (for instance, in cardiac decompensation with oedema) may perhaps seriously influence the initial neck curve, a factor which must be thoroughly investigated.

SUMMARY

Continuous registration of the counting rates over the neck following the intravenous injection of I^{131} was carried out by means of a scintillation counter combined with a counting-rate meter and a writing instrument. The resulting 'initial neck curve' gave good information about the iodine-concentrating capacity of the thyroid as early as 5 to 10 minutes after the injection. The practical and theoretical advantages of the test are discussed.

ZUSAMMENFASSUNG

Kontinuierliche Registrierung der Messausschläge über dem Hals nach intravenöser Injektion J^{131} wurde mit Hilfe eines Szintillationszählers, der mit einem Impulsmessgerät und einem Schreibinstrument verbunden ist, ausgeführt. Die sich daraus ergebende »initiale Halskurve« gab schon 5—10 Minuten nach der Injektion gute Auskunft über das Jodkonzentrationsvermögen der Thyreoidea. Die praktischen und theoretischen Vorteile des Testes werden besprochen.

RÉSUMÉ

Le taux de comptage sur le cou après injection intraveineuse d'I^{131} a été enregistré de façon continue au moyen d'un compteur à scintillation combiné à un appareil de mesure et à un système d'inscription. La «courbe cervicale initiale» a fourni de bons renseignements sur la capacité de concentration de l'iode de la thyroïde dès la 5e à la 10e minute après l'injection. Les auteurs discutent les avantages pratiques et théoriques de ce test.

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THE EFFECT OF HIGH AND LOW ROENTGEN INTENSITY ON DOMINANT LETHALS IN DROSOPHILA MELANOGASTER

by

K. G. Lüning, Bo Lindell and *R. Falk.*

By means of a new type of roentgen ray equipment (SIEVERT; 4) it is possible to deliver (in a small volume inside the anode) doses up to 1,000 r within 50 microseconds. It was therefore of interest to study the biologic effectiveness of irradiation with such a high intensity as compared to the usual low intensities employed in most experiments.

In studies of roentgen ray induced chromosome damage (breaks) in Drosophila sperms, LÜNING (2, 3) has shown that the maximum rate was obtained in spermatozoa as early as 7 to 10 days after irradiation of 0—1 day old males. Eggs fertilized by spermatozoa irradiated with 1,000 r in this sensitive stage showed a hatchability of about 40 to 50 per cent as compared to the control rate around 90 to 95 per cent. Since we could not produce much more than 1,000 r at a maximum in each treatment, this sensitive stage seemed to us convenient to use in a test of the high intensity irradiation.

In order to determine the effect of intensity on chromosome breaks, each treatment at high intensity was paralleled by a treatment at low intensity with a Maximar apparatus. This latter produced roentgen radiation of about the same quality as that of high intensity but with a dose rate of only 50 r/min. The Maximar treatments thus had a duration of the order of 15 minutes and we could utilize a ratio of irradiation times of about 10^7.

We treated wild type males from the Canton S stock, 3 to 22 hours old. They were divided without etherization into two portions and

Submitted for publication, 18 June 1954.

placed in lucite cups. In the high intensity treatment two ionization chambers were attached vertically on the top of the cup which was irradiated from the surrounding cylindrical transmission target. Within 5 to 10 minutes, the second group was treated with a similar dose but at low intensity.

As the same ionization chambers were used for both high and low intensity irradiation, and the radiation qualities were essentially similar (the condensers used in connection with the high-intensity tube were charged to 365 kV, but the radiation was heavily filtered by the transmission target; the operation voltage with the Maximar was 370 kVp), the measured dose values are comparable with a rather high degree of accuracy; the relation between the actual absolute dose level and the chamber ionization may, however, be somewhat uncertain.

We used condenser ionization chambers of the SIEVERT type (5), modified (by Dr. R. THORAEUS) to a higher capacitance and hence capable of measuring up to 1,000 r. A dose correction was estimated due to the fact that the chambers were placed at some distance from the irradiated volume. Another correction had to be made to eliminate the influence of ionization loss caused by recombination of ions in the chamber at the high intensity. The method used has been described by LINDELL (1) in a paper which gives also a description of the dose distribution in the irradiated volume in the discharge tube. He found rather a high recombination, corresponding to about 20 per cent at the doses used in this investigation, but we have used chambers with shorter electrode distances (0.7 mm) and hence with only around 4 per cent ionization loss.

Every dose was calculated from the average values of the two chambers which were irradiated simultaneously. The statistical mean error of this estimation has been shown, from a long series of measurements, to be about 2 per cent. A reasonable upper limit for the numerical value of the systematical error, however, cannot be considered to be lower than approximately 4 per cent. This is of course valid for the relative measurements only and consequently the real dose level becomes even more uncertain. The figure of 4 per cent is to be taken as a limit based upon the authors' experience and is difficult to present in an objective way. The estimated maximum systematic error is in fact + 15 to — 6 per cent.

The irradiated males were mated to unselected females for 6 days. At the beginning of the 7th day they were mated in pairs to F_1 daughters from the cross cn bw; e^{11} ♀♀ × Canton S ♂♂. According to STRÖMNÆS (6) these females have a high egg-laying capacity with a high rate of hatchability when mated to untreated males — above 95 per cent. Eggs were collected for four consecutive days. The rate of hatchability was calculated from pairs which had produced larvae from the eggs laid in a

preceding day. The experiment was repeated three times. The results are presented in Diagram 1 and Table 1.

The physical and the biologic errors (which are of the same order) make the small difference inconclusive as regards establishment of a dif-

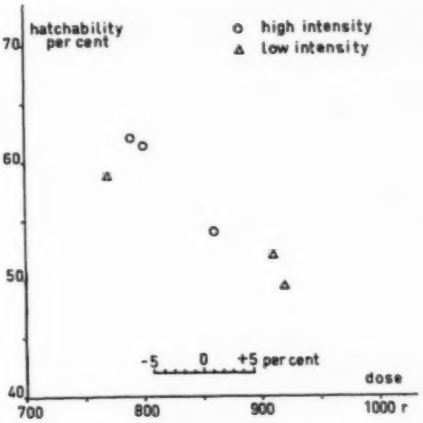

Diagram 1.

ference in intensity effect. One may, however, say that high intensity radiation seems not to have, within the limits given by the systematic errors in this experiment, any differential effect in inducing dominant lethals than irradiation of low intensity.

Table I

Experiment number	High intensity			Low intensity		
	Dose (r)	Number of eggs	Rate of hatchability in %	Dose (r)	Number of eggs	Rate of hatchability in %
I	800	4,314	61.4	770	4,208	58.8
II	860	6,206	54.0	910	4,879	52.0
III	790	3,438	62.1	920	4,529	49.4

SUMMARY

By means of a discharge roentgen tube, earlier described by SIEVERT, the authors have tested the biologic effectiveness of high intensity radiation. *Drosophila* males were irradiated with 800 to 900 r and after 7 days, *i. e.* during a period of maximum chromosome damage rate, mated to selected females of high egg-laying capacity. No significant difference in hatchability could be seen when high as compared to low intensity radiation was used, though the high intensity produced the irradiation dose within only 50 microseconds and the low intensity dose was given over 15 minutes.

ZUSAMMENFASSUNG

Mit Hilfe einer von SIEVERT früher beschriebenen Entladungsröntgenröhre haben die Verfasser die biologische Wirksamkeit von Strahlung hoher Intensität getestet. Drosophila Männchen wurden mit 800 bis 900 r bestrahlt und nach 7 Tagen, d. h. während einer Periode maximaler Chromosomenschädigung, mit auserwählten Weibchen mit hoher Eierlegekapazität gepaart. Kein signifikativer Unterschied in der Ausbrütungskapazität konnte bei Benutzung von Strahlung hoher oder niedriger Spannung beobachtet werden, obgleich hohe Spannung die Strahlendosis innerhalb von nur 50 Mikrosekunden erzeugte, während bei niedriger Spannung die Dosis erst nach mehr als 15 Minuten erreicht wurde.

RÉSUMÉ

Utilisant un tube roentgen à décharge décrit par SIEVERT, les auteurs ont testé l'action biologique des rayons à haute intensité. Des *Drosophiles* mâles ont reçu 800 à 900 r et, 7 jours plus tard, c'est-à-dire à une période où le taux des lésions chromosomiques est maximum, ont été accouplées à des femelles sélectionnées de grande fécondité. On n'a pas observé de différence importante du taux des éclosions sous les effets comparés des radiations de haute et de basse intensité, bien que la haute intensité fournît la dose d'irradiation en 50 microsecondes seulement et que la dose à basse intensité fût donnée en plus de 15 minutes.

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BOOK REVIEWS

CHOLESTEATOMA OF THE MIDDLE EAR. A Clinical and Roentgenologic Study. By Lars Winderen and Johannes Zimmer. 119 pp, 45 figures (122 roentgenograms), 35 tables. Acta radiol. Suppl. 111. Stockholm 1954. Sw. Kr. 20: —.

This work deals only with the so-called 'pseudo-cholesteatoma' or 'false cholesteatoma', by pathologists sometimes termed 'epidermoid cyst'. The study does not cover the so-called 'true cholesteatoma' — frequently situated outside the temporal bone.

The authors have reviewed 536 temporal bones in 523 patients suffering from chronic middle ear infection. Available roentgenograms from 200 of these patients have been studied closely.

All the patients were admitted and treated at the Department of Oto-Laryngology, and the radiologic examination carried out at the Department of Radiology, University Hospitals, Oslo, during the eleven-year-period from 1940 to the end of 1950.

The *clinical section* covers the first 32 pages. In a separate chapter emphasis is laid on indications for surgical intervention in chronic middle ear infection, with special consideration to the extent to which the preoperative roentgen findings aided the surgeon as an indication for operation. In a rather high proportion of cases the roentgen reports supported the necessity for operative intervention.

Another chapter deals with the various types of pneumatization of the temporal bone in relation to age of onset of otogenic complications. The pneumatization of the opposite temporal bone is also recorded and discussed.

The extent of the pneumatic cell system on the operated side is divided into five groups as used at the Department of Radiology of the University Hospitals, Oslo. Restricted pneumatization was by far the most common group. The pneumatization of the non-operated temporal bones was more evenly distributed among the different groups.

A rather high incidence of otogenic complications was found — and was surprisingly high when the pneumatic cell system was well developed. In this material it was obvious that the more highly developed the cell system the greater the tendency towards serious complications.

The material further shows that if marginal perforation of the ear drum was present and aural discharge had lasted for a certain number of years, the risk of serious complications was sufficiently great to warrant surgical intervention.

The average duration of aural discharge was longest in cases belonging to the non-pneumatized temporal bone. Otogenic complications occurred with the highest frequency in cases with cholesteatoma involving the antral region. A connection between the size of a cholesteatoma and otogenic complications was also recorded.

As far as the clinical evaluation of the cases was concerned, the sedimentation rate was found to be of secondary importance.

In the *roentgenologic section*, the value of the roentgen examination, general principles of the roentgenologic diagnosis of cholesteatoma of the middle ear, and some technical sources of error regarding the projections employed, are considered.

The roentgenologic material comprises 200 temporal bones examined, six to eight different projections for each case being employed. In 131 temporal bones, a finding of

cholesteatoma was made operatively; in 45 cases, no cholesteatoma was present at operation. A roentgenologic comparison as precise as possible, is made between these two groups, the size of the cholesteatomas also being taken into consideration. The main group with operative findings of cholesteatoma is subdivided according to where the cholesteatoma was found at operation, in the antrum, and/or aditus ad antrum, and/or attic regions. The possibilities of diagnosing a cholesteatoma situated in one or more of these areas were carefully studied and recorded. Furthermore, the size of the cholesteatomas was found to influence the diagnostic possibilities.

In the smaller group of 45 cases in which no cholesteatoma was found at operation, the condition was difficult to exclude roentgenologically in 18 cases. A number of these cases is recorded and discussed.

A special investigation of the mastoid antrum as seen in the fronto-occipital projection was carried out. The shape and size of the antrum in this projection was of considerable diagnostic help to the roentgenologist on a great many occasions. A large number of antra were evaluated in this projection and, when possible, measured in different diameters. The measurements are given in tables, and conclusions drawn.

Otogenic complications both in cases with and without cholesteatoma are recorded.

In the last part of the book, one chapter deals with certain cases in which the operation finding was 'cholesterol granuloma', *i. e.* granulation tissue mixed with crystals of cholesterol. A few cases indicated an expansive lesion in the tympanum. Another chapter deals with a group of previously operated temporal bones more particularly regarding the problems of diagnosing a cholesteatoma. The diagnostic possibilities are limited.

Planigraphy of the temporal bone in middle ear infection was carried out in a restricted number of cases. In doubtful cases, it was found to support or confirm the diagnosis. The anatomy of the temporal bone is well demonstrated by planigraphy, thus aiding the surgeon in difficult cases.

In the last chapter previous films of six patients are compared with recent roentgenograms in order to determine how fast a cholesteatoma expands. One case with marked expansion, 17 years after the first films were taken, is recorded.

The various chapters in the roentgenologic section are supplied with illustrative case reports, 41 in all, as well as numerous roentgenograms in different projections.

Autoreview.

RADIOLOGIE CLINIQUE DE L'INTESTIN GRÊLE DE L'ADULTE ET DE L'ENFANT. Par P. Porcher, P. Buffard et J. Sauvegrain. 614 pages, 3,500 illustrations. Masson & Cie, Paris 1954. Frcs. 5,000: —.

The work deals with the clinical, pathologico-anatomic and roentgenologic aspects of the subject. A survey of the literature is contained in every chapter. The illustrations are quite independent of the text but each legend includes the clinical data with a summary in English. The diagnosis has been verified in most cases by operation and microscopic investigation and in the others by the clinical course of the condition.

The technique of examination is described in detail. The author's account of his own experiences of the effects of various drugs upon the tone and motility of the wall of the bowel and thus in the assessment of its organic condition, is of special interest. In the discussion upon the appearance of gas in the small intestine, the diagnostic value of constant gas-containing of a certain portion of the bowel is pointed out. This may constitute an indirect sign of a pathologic change in a neighbouring organ and have either a functional or organic cause.

The diagnostics of the small intestine in children, with special reference to mal-

formations, invaginations, adenopathy and meconium ileus, are dealt with in a special chapter.

In individual chapters, the authors attempt to work out the foundation for, and the reliability of, the roentgen picture in 'functional insufficiency' of the small intestine in various kinds of nutritional disorders (dystonia, disturbances of peristalsis and of the relief of the mucosal pattern, fluid retention with clouding of the barium). The description of an allergic condition in the small intestine with radiologic findings of oedema of the folds, disorders in the absorption of fluids and gases, is of special interest.

The diagnostics of tumours, tuberculosis, as well as post-operative conditions are also described. Regional enteritis is illustrated in detail by four cases, one of which was cured after an observation period of four years.

The book is based upon the great experience of the authors. The picture material is first-class and the review of the literature exhaustive. The work thus forms a valuable handbook in a large and difficult field of roentgen diagnostics.

Folke Knutsson.

BOOKS RECEIVED

We acknowledge with thanks under this heading books received for review, which we trust will be regarded as a sufficient mark of appreciation of the courtesy of the sender. The reviews of selected items will appear as soon as opportunity affords.

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